IMMUNOHISTOCHEMICAL SPECTRUM OF MESENCHYMAL TUMORS

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I hereby declare that the thesis entitled "**IMMUNOHISTOCHEMICAL SPECTRUM OF MESENCHYMAL TUMORS**" submitted towards partial fulfillment of the requirements for the award of **MD in Pathology** degree to BFUHS is a compilation of original work carried out by me under the supervision of Dr Neena Sood, Former Professor & Head, Dr. Sumit Grover, Associate Professor, Department of Pathology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my Family

&

Teachers

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ABBREVIATIONS

WHO: World Health Organization

PNET: Primitive Neuroectodermal Tumor

ES: Ewing's Sarcoma

STT: Soft Tissue Tumors

IHC: Immunohistochemistry

WDLS: Well-Differentiated Liposarcoma

DDLS: De-Differentiated Liposarcoma

MSA: Muscle Specific Actin

SFT: Solitary Fibrous Tumor

IMT: Inflammatory Myofibroblastic Tumor

DFSP: Dermatofibrosarcoma Protuberans

RM: Rhabdomyoma

RMS: Rhabdomyosarcoma

ERMS: Embryonal Rhabdomyosarcoma

ARMS: Alveolar Rhabdomyosarcoma

LM: Leiomyoma

LMS: Leiomyosarcoma

AVH: Arteriovenous Hemangioma

VH: Venous Hemangioma

KS: Kaposi Sarcoma

EHE: Epithelioid Hemangioendothelioma

PNST: Peripheral Nerve Sheath Tumor

MPNST: Malignant Peripheral Nerve Sheath tumor

GIST: Gastrointestinal Stromal Tumor

SS: Synovial Sarcoma

STS: Soft Tissue Sarcoma

ESS: Endometrial Stromal Sarcoma

H & E: Hematoxylin and Eosin

EMA: Epithelial Membrane Antigen

CK: Cytokeratin

h-CD: High Molecular Weight Caldesmon

SMA: Smooth Muscle Actin

CD: Cluster of Differentiation

DOG1: Discovered On Gist 1

ER: Estrogen receptor

LCA: Leucocyte Common Antigen

MDM2: Murine Double Minute Type 2

ABSTRACT

Introduction: IHC is a widely used technique in diagnostics and research and its application continue to extend because of its ease to use, reliability and versatility. Advantage of this technique is visible morphology of tissue around the specific antigen by counter staining.

Aim of study: To study immunohistochemical spectrum of mesenchymal tumors.

Materials and methods-The present study was a prospective and retrospective study on immunohistochemical spectrum of mesenchymal tumors of specimens received in the Department of Pathology, Dayanand Medical College & Hospital, Ludhiana over a period of 5 years (3.5 years retrospectively from 1st July 2016 to 31st December 2019 and 1.5 years prospectively from 1st January 2020 to 30th June 2021). During this period all the specimens were analyzed with respect to light microscopic and IHC findings for mesenchymal tumors.

Results: During the study period a total of 442 cases of mesenchymal tumors were received for histopathological examination in our department. Out of these, 185 cases of immunohistochemically confirmed mesenchymal neoplasms were analyzed with respect to light microscopic and immunohistochemical findings. It was observed that the mesenchymal neoplasms occurred more often between 5^{th}-7^{th} decade with the mean age of 48.3 years. The most common group of tumors were smooth muscle tumors [n = 48] followed by GIST [n = 36]. On immunohistochemical examination, amongst smooth muscle tumors, SMA & h-caldesmon were found to be the most sensitive markers, both showing 100% positivity in case of leiomyoma and 97.4% & 100% positivity respectively, in case of LMS. DOG-1 and C-kit were consistently found to be positive in GIST in 100% and 93.4% cases respectively. In fibroblastic and myofibroblastic tumors, All the cases of solitary fibrous tumors showed 100% positivity for vimentin, CD34, Bcl2 and CD 99. CD34 was found to be consistently positive in all the cases of DFSP [6/6]. All the cases of PNSTs showed 100% positivity for S-100. All the cases of RMS were 100% positive for vimentin, desmin and myogenin. MDM2 showed 100% positivity in cases of liposarcoma. In our study , all the cases of ES/PNET showed 100% membranous positivity for CD99. Synovial sarcomas showed 100% positivity for vimentin, with CK and EMA showing 77.87% and 57.14% positivity respectively. Glomus tumor and angioleiomyoma showed SMA and CD34 positivity while, myopericytoma showed positivity for h-caldesmon and was negative for CD34.

Conclusion: Although histopathological examination is considered gold standard in the diagnosis of mesenchymal tumors, IHC is of immense value in arriving at a final diagnosis, specially when faced with a malignant spindle cell neoplasm of a tumor having pleomorphic morphology.The combination of morphology and judicious use of IHC markers help us to arrive at a final diagnosis.

Keywords: Histopathology, immunohistochemistry, mesenchymal neoplasms.

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INTRODUCTION

The greatest amount of bulk of the body is composed of the cells forming tissues that are considered "*soft tissues*" or connective tissues. These are embryologically derived from the *mesoderm*. Hence, they are often called "*mesenchymal*" *tissues*.

Soft tissue tumors are defined as mesenchymal proliferations that occur in soft tissue which is non-epithelial extra skeletal tissue of body exclusive of reticuloendothelial system, glia and supporting tissue of various parenchymal organs. Soft tissue is represented by voluntary muscles, fat and fibrous tissue along with vessels.[1]

Tumors arising from these are called Mesenchymal tumors. Soft tissue tumors have wide morphological and histological variation that can be detected by microscopic examination. As benign soft tissue tumors outnumber their malignant counterpart, these tumors mostly resemble the normal tissues.[2] There are ancillary techniques that have been successfully applied to increase diagnostic accuracy; these include conventional special stains, electron microscopy, immunohistochemistry and cytogenetic /molecular methods. These tumors arise nearly anywhere in the body, the most important locations being the extremities, trunk, abdominal cavity and head &neck.[2] There is no known predisposing cause but majority of them arise sporadically. Unlike carcinomas that usually arise from recognized precursor lesions; the origin of sarcomas is unknown. Reports have linked specific genetic, immunodeficiency, viral infection and environmental factors with the development of some sarcomas. Environmental factors (e.g., radiation, herbicides) have been associated with the development of specific types of sarcomas.[3-7] Some sarcomas have a higher predisposition to occur in the setting of familial cancer syndromes (e.g., retinoblastoma syndrome, Li-Fraumeni syndrome, hereditary leiomyomatosis and renal cell carcinoma).[8-11] These observations suggest that both environmental and genetic factors are important in the development of these tumors.

2013 World Health Organization (WHO) classification of tumors of soft tissue arranges these tumors into 12 groups according to their histiogenesis as follows: adipocytic, fibroblastic/myofibroblastic, fibrohistiocytic, smooth muscle, pericytic (perivascular), skeletal-muscle, vascular, gastrointestinal stromal, nerve sheath, uncertain differentiation, and undifferentiated/unclassified.[12] Tumor behavior is classified as benign, intermediate (locally aggressive), intermediate (rarely metastasizing), and malignant. The WHO classifies mesenchymal tumors based on various histological patterns. Adipocytic tumors include lipoma (benign), liposarcoma; Fibroblastic tumors includes myofibroma, fibrosarcoma, Desmoid type fibromatosis; vascular tumors include hemangioma, lymphangioma, angiosarcoma. Soft tissue tumors arising from skeletal muscle are Rhabdomyoma, rhabdomyosarcoma and that arising from smooth muscle include Leiomyoma, leiomyosarcoma. Apart from these some soft tissue tumors are of uncertain differentiation, these include Myxomas, synovial sarcoma, primitive neuroectodermal tumor (PNET).[12]

Although pathologically diverse, Mesenchymal tumors frequently exhibit similar clinical presentations and radiological features. Correct histopathological and immunophenotypic diagnosis is therefore crucial.

In today's practice, a general approach to reaching a definitive diagnosis of soft tissue tumors is to first evaluate clinico-radiological, histomorphological, and cytomorphological features of the tumor to generate a differential diagnosis. These include the potential line of histogenesis and whether the tumor is benign or malignant, and low or high grade. Although molecular/genetic testing is increasingly finding its applications in characterizing soft tissue tumors, currently *immunohistochemistry* still not only plays an indispensable role in defining tumor histogenesis, but also serves as a surrogate for underlining molecular/genetic alterations. In the current study we have assessed the immunohistochemical spectrum of soft tissue tumors.

AIMS AND OBJECTIVES

To study the immunohistochemical spectrum of mesenchymal tumors**.**

REVIEW OF LITERATURE

Soft tissue tumors (STT) are mesenchymal neoplasms with a diverse spectrum and overlapping clinical, radiological and histological features. Mesenchymal tumors are not a common biopsy material of surgical pathology. Enzinger F.M. & W.W. Weiss 1983, Robbins et al 1994, Myhre Jenson et al 1981 reported an incidence of soft tissue tumors as 0.8-1%, 0.8% and < 2% respectively. Benign soft tissue tumors are more common than malignant. The most common benign tumors are lipoma (44.5%) followed by hemangioma (14.0%) and schwannoma (5.5%).[13] The bulk of intermediate tumors are formed by fibromatosis, hemangioendothelioma and giant cell tumor of soft tissue. The commonest malignant tumors are sarcomas NOS followed by leiomyosarcoma. The benign tumors are found to be commoner in younger population whereas malignant tumors are seen in 5th to 6th decade. Statistically highly significant correlation is found between age and the category of tumor. The most common site of soft tissue tumors as a whole is head & neck (29.0%) followed by upper limb (25.5%).[13] Among benign tumors, hemangiomas have a predilection for head &neck while lipomas are seen commonly in upper limb. Most favoured site for sarcomas is lower limb, followed by abdomen.

Soft tissue sarcomas seem to show an upward trend, possibly because of increase in incidence, rising interest in tumor and better diagnostic capabilities.

WHO CLASSIFICATION

The 5th edition of the World Health Organization (WHO) classification of soft tissue and bone was published in April 2020.[14] Since the publication of the 4th edition in 2013,[12] considerable advances have been made in our understanding of many soft tissue tumors, namely in the form of newly recognized molecular and genetic alterations, immunohistochemical markers, and biological mechanisms. The new 2020 WHO classification follows the same organization as the previous (4th) edition, describing the following lineage groups: (1) adipocytic tumors, (2) fibroblastic and

myofibroblastic tumors, (3) so-called fibrohistiocytic tumors, (4) vascular tumors, (5) pericytic (peri-vascular) tumors, (6) smooth muscle tumors, (7) skeletal muscle tumors, (8) gastrointestinal stromal tumors (GISTs), (9) chondro-osseous tumors, (10) peripheral nerve sheath tumors, and (11) tumors of uncertain differentiation. A new chapter describing undifferentiated small round cell sarcomas of bone and soft tissue has been introduced.Tumor behavior is classified as benign, intermediate (locally aggressive), intermediate (rarely metastasizing), and malignant.[14]

Soft tissue tumors (STTs) are a complex group of pathologically diverse childhood and adult neoplasms with differentiation towards mesenchymal tissue, which may arise almost anywhere in the body.[15] A general approach to reaching a definitive diagnosis when involving soft tissue tumors is to first consider clinic-radiologic, histomorphologic, and cytomorphologic features of the tumor to generate a pertinent differential diagnosis that includes the potential line of histogenesis and whether the tumor is benign or malignant.

Sometimes, the line of histologic differentiation is obvious such as smooth-muscle, skeletal-muscle, vascular, neural, and chondro-osseous lineages. However, when the line of differentiation is not obvious, the histomorphological pattern encountered may help in determining differential diagnoses for further workup.

Ancillary testing is often required to confirm the tumor histogenesis when working up a soft tissue tumor. Immunohistochemistry (IHC) plays an important role in the diagnosis of soft tissue tumors. The ultimate goal for a pathologist is to render a specific diagnosis that provides diagnostic, prognostic, and therapeutic information to guide patient care. Overlap between clinical, radiological and histological patterns of benign, malignant and non-malignant lesions makes careful histopathological examination with supportive investigations like IHC almost essential in many cases.[16]

WHO CLASSIFICATION OF TUMORS OF SOFT TISSUE & BONE 2013

ADIPOCYTIC

Benign

Lipoma

Lipomatosis

Lipomatosis of nerve

Lipoblastoma / lipoblastomatosis

Angiolipoma

Myolipoma of soft tissue

Chondroid lipoma

Extra-renal angiomyolipoma

Extra-adrenal myelolipoma

Spindle cell / pleomorphic lipoma

Hibernoma

Intermediate (locally aggressive)

Atypical lipomatous tumor / well differentiated liposarcoma

Malignant

Dedifferentiated liposarcoma

Myxoid liposarcoma

Pleomorphic liposarcoma

Liposarcoma, not otherwise specified

Fibroblastic &myofibroblastic tumors

Benign

Nodular fasciitis

Proliferative fasciitis

Proliferative myositis

Myositisossifficans

Fibro-osseous pseudotumor of digits

Ischemic fasciitis

Elastofibroma

Fibrous hamartoma of infancy

Fibromatosis colli

Juvenile hyaline fibromatosis

Inclusion body fibromatosis

Fibroma of tendon sheath

Desmoplastic fibroblastoma

Mammary-type myofibroblastoma

Calcifying aponeurotic fibroma

Angiomyofibroblastoma

Cellular angiofibroma

Nuchal-type fibroma

Gardner fibroma

Calcifying fibrous tumor

Intermediate (locally aggressive)

Palmar / plantar fibromatosis

Desmoids-type fibromatosis

Lipofibromatosis

Giant cell fibroblastoma

Intermediate (rarely metastasizing)

Dermatofibrosarcoma protuberans

- Fibrosarcomatous dermatofibrosarcoma protuberans
- Pigmented dermatofibrosarcoma protuberans

Solitary fibrous tumour

- Solitary fibrous tumour, malignant

Inflammatory myofibroblastictumour

Low grade myofibroblastic sarcoma

Myxoinflammatory fibroblastic sarcoma /

- Atypical myxoinflammatory fibroblastic tumor

Infantile fibrosarcoma

Malignant

Adult fibrosarcoma

Myxofibrosarcoma

Low-grade fibromyxoid sarcoma

Sclerosing epithelioid fibrosarcoma

So-called fibrohistiocytictumors

Benign

Tenosynovial giant cell tumor

- Localized type
- Diffuse type
- Malignant

Deep benign fibrous histiocytoma

Intermediate (rarely metastasizing)

Plexiform fibrohistiocytictumor

Giant cell tumor of soft tissue

Smooth-muscle tumors

Benign

Leiomyoma of deep soft tissue

Malignant

Leiomyosarcoma

Pericytic (perivascular) tumors

Glomus tumor (and variants)

- Glomangiomatosis
- Malignant glomus tumor

Myopericytoma

- Myofibroma
- Myofibromatosis

Angioleiomyoma

Skeletal-muscle tumors

Rhabdomyoma

Embryonal rhabdomyosarcoma

Alveolar rhabdomyosarcoma

Pleomorphic rhabdomyosarcoma

Spindle cell / Sclerosing rhabdomyosarcoma

Vascular tumors

Benign

Haemangioma

- Synovial
- Venous
- Arteriovenous haemangioma / malformation

Epithelioid haemangioma

Angiomatosis

Lymphangioma

Intermediate (locally aggressive)

Kaposiformhaemangioendothelioma

Intermediate (rarely metastasizing)

Retiform haemangioendothelioma

Papillary intralymphaticangioendothelioma

Composite haemangioendothelioma

Pseudomyogenic (epithelioid sarcoma-like) haemangioendothelioma

Kapsoi sarcoma

Malignant

Epithelioid haemangioendothelioma

Angiosarcoma of soft tissue

Gastrointestinal stromal tumors

Benign gastrointestinal stromal tumor

Gastrointestinal stromal tumor, uncertain malignant potential

Gastrointestinal stromal tumor, malignant

Nerve sheath tumors

Benign

Schwannoma (including variants)

Melanotic schwannoma

Neurofibroma (including variants)

- Plexiform neurofibroma

Perineurioma

Malignant perineurioma

Granular cell tumor

Dermal nerve sheath myxoma

Solitary circumscribed neuroma

Ectopic meningioma

Nasal glial heterotopia

Benign Triton tumor

Hybrid nerve sheath tumors

Malignant

Malignant peripheral nerve sheath tumor

Epithelioid malignant nerve sheath tumor

Malignant Triton tumor

Malignant granular cell tumor

Ectomesenchymoma

Tumors of uncertain differentiation

Benign

Myxoma NOS

Aggressive angiomyxoma

Pleomorphic hyalinizing angiectatictumor

Perivascular epithelioidtumor,benign

Intermediate (locally aggressive)

Haemosideroticfibrolipomatoustumor

Intermediate (rarely metastasizing)

Atypical fibroxanthoma

Angiomatoid fibrous histiocytoma

Ossifying fibromyxoidtumor

Ossifying fibromyxoidtumor, malignant

Mixed tumor NOS

Mixed tumor NOS, malignant

Myoepithelioma NOS

Malignant

Synovial sarcoma NOS

Synovial sarcoma, spindle cell

Synovial sarcoma, biphasic

Epithelioid sarcoma

Alveolar soft-part sarcoma

Clear cell sarcoma of soft tissue

Extraskeletal myxoid chondrosarcoma

Extraskeletal Ewing sarcoma

Desmoplastic small round cell tumor

Neoplasms with perivascular epithelioid cell differentiation (PEComa)

Spindle cell sarcoma,undifferentiated

Pleomorphic sarcoma, undifferentiated

Round cell sarcoma, undifferentiated

Adipocytic tumors

Benign

Lipoma

Conventional lipoma is composed of lobules of mature adipocytes. The cells are identical to surrounding adipose tissue except for slight variation in size and shape of cells. Intramuscular lipomas may either be well demarcated from the surrounding skeletal muscle or often shows an infiltrative growth pattern with mature adipocytes infiltrating skeletal muscle bundles.[17]

Lipomatosis

Lipomatosis is a diffuse overgrowth of mature adipose tissue. It occurs in a variety of clinical setting and affects different anatomic regions of the body. Diffuse lipomatosis involves the trunk, large portion of extremity, head and neck, abdomen etc.

Lipoblastoma/lipoblastomatosis

A lobulated localized (lipoblastoma) or diffuse (lipoblastomatosis) tumor, resembling fetal adipose tissue. Patients present with a slowly growing

soft tissue nodule or mass, well circumscribed and confined to the subcutis in case of lipoblastoma, infiltrating the deeper muscle in case of lipoblastomatosis. Lipoblastoma shows a lobulated appearance with an admixture of mature and immature adipocytes, the latter corresponding to lipoblasts in various stages of development.[18]

Pleomorphic lipoma/ spindle cell lipoma

The classic spindle cell lipoma consists of a relative equal mixture of mature fat and spindle cells. The spindle cells are uniform with a single elongated nucleus and narrow bipolar cytoplasmic processes. Nucleoli are inconspicuous. The classic pleomorphic lipoma is characterized by the presence of scattered, bizarre giant cells that frequently have concentric floret like arrangement of multiple hyperchromatic nuclei and deeply eosinophilic cytoplasm along with presence of collagen bundles.[19] This neoplasm is characterized by an admixture of variably sized adipocytes and bizzare, pleomorphic , multinucleated giant cells many of which show floret like arrangement of nuclei and are associated with interlacing bundles of collagen.[20]

Intermediate

Atypical lipomatous tumor/well differentiated liposarcoma

Atypical lipomatous tumor is an intermediate malignant mesenchymal neoplasm composed of either entirely or in part of a mature adipocytic differentiation showing significant variation in cell size and focal nuclear atypia in both adipocytes and stromal cells. It is composed of small and large adipocytes with interspersed fibrous septa that contain large, irregular, hyperchromatic nuclei. Small nucleoli in some of the large cells.[21]

Malignant

Dedifferentiated liposarcoma

It is a high-grade malignancy of the deep soft tissue and retroperitoneum that can arise de novo or by transformation of WDLS. Compared to its well differentiated counterpart, DDLS is a highly cellular tumor composed of at

least mildly pleomorphic cells that bear no resemblance to mature adipocytes. This neoplasm can exhibit an impressive variety of cytomorphologic features and architectural arrangements, including spindled, epithelioid, fascicular, storiform, and myxoid patterns. Often numerous mitoses and areas of necrosis are seen.

DDLS can undergo “heterologous differentiation,” transformation into a high-grade sarcoma of another cell lineage, such as leiomyosarcoma, rhabdomyosarcoma, osteosarcoma, orchondrosarcoma. While the varied histologic manifestations of DDLS can create diagnosticchallenges, detection of MDM2 and CDK4 amplification (a feature shared by WDLS and DDLS) can aid in diagnosis.[22]

Myxoid liposarcoma

Myxoid liposarcoma is a translocation associated neoplasm that accounts for roughly one-third of liposarcomas. Classically, it occurs within the deep soft tissue of the extremities and, unlike WDLS and DDLS, rarely arises in the retroperitoneum. This tumor forms a lobulated mass and has distinctive light blue “myxoid” stroma and a network of delicate branching capillaries that has been compared to chicken wire. Two predominant histological types of tumor cells are found: small, bland, spindle-shaped mesenchymal cells, and a variable number of uni or multivacuolated lipoblasts. Mitotic activity and nuclear pleomorphism are generally minimal.

Fibroblastic and myofibroblastic tumors

Benign

Nodular fasciitis

Nodular fasciitis is a mass forming fibrous proliferation that usually occurs in the subcutaneous tissue. Microscopically it is composed of plump but regular spindle-shaped fibroblasts (or myofibroblasts) lacking nuclear hyperchromasia and pleomorphism. Mitotic figures may be plentiful, but atypical mitosis is not seen.

Immunohistochemically – stains for smooth muscle actin (SMA) and muscle specific actin (MSA) are usually positive, but desmin positivity is rare.[23]

Fibromatosis coli

It is defined as site-specific lesion that occurs in the distal sternocleidomastoid muscle of infants. In these the lesion is composed of uniform plump fibroblastic and myofibroblastic cells embedded in collagenous background. Infiltration and entrapment of skeletal myocytes is evident.

Immunohistochemistry- The cells exhibit positive staining for vimentin and muscle actins.[24]

Intermediate (locally aggressive)

Superficial fibromatosis

Superficial fibromatosis are fibroblastic proliferations that arise in the palmar or plantar soft tissue and have infiltrative growth pattern.

The proliferative phase is characterized by proliferation of plump, immature-appearing spindled cells that are small in size and shape, have normochromatic nuclei and small nucleoli. Mitotic figures are usually absent. Cells are closely associated with moderate amounts of collagen and elongated vessels. Older lesions are considerably less cellular and have increased amounts of dense collagen.

Immunohistochemistry- the cells strongly express vimentin and variably stain for muscle-specific and smooth muscle actin.[25]

Desmoid type fibromatosis

Desmoid-type fibromatosis are fibroblastic proliferations that arise in the deep soft tissue and are characterized by infiltrative growth and tendency toward local recurrence, but does not metastasize. It is characterized by a proliferation of elongated, slender, spindle-shaped cells of uniform appearance, present in a collagenous stroma containing variable number of prominent vessels. Cells are usually arranged in sweeping bundles.

Immunohistochemistry- the cells strongly express vimentin and variably stain for muscle-specific and smooth muscle actin.[26]

Intermediate (rarely metastasizing)

Solitary fibrous tumor

Solitary fibrous tumor (SFT) is a fibroblastic neoplasm of adults with a wide distribution and a benign clinical course in the majority of cases, although up to one-fourth metastasize. These hypercellular tumors have been described as having a “pattern-less pattern” of bland spindle-shaped fibroblasts with hypocellular and hypercellular zones, set within a collagenous stroma. Dilated, branching blood vessels with the appearance of ramifying antlers or horns are a distinctive feature. SFTs can rarely transform into a high-grade de-differentiated sarcoma with anaplastic and heterologous elements.[27,28]

No single histologic feature correlates with aggressive or malignant behavior, and even histologically benign SFTs can recur and metastasize. A risk assessment model incorporating patient age, tumor size, mitotic activity, and tumor necrosis provides a reasonably powerful prediction of tumor behavior.[29,30] SFT is characterized by an intrachromosomal inversion of chromosome 12 resulting in fusion of NAB2 and STAT6 [31], which manifests with STAT6 over-expression by immunohistochemistry.[32] These tumors are characteristically immunoreactive for CD34 and CD99.[33]

Inflammatory myofibroblastic tumor

Inflammatory myofibroblastic tumor (IMT) is a spindle cell neoplasm of intermediate malignant potential that occurs in the lungs, mesentery, and omentum of children and young adults, with a slight female predominance.[34] Histologically, IMT is composed of spindled myofibroblasts, fibroblasts, and a characteristic inflammatory infiltrate of plasma cells, lymphocytes, andeosinophils. The tumor assumes 3 main histologic appearances: loosely arranged spindle cells in an edematous and myxoid stroma, spindle cells in fascicles with aggregatesof plasma

cells, and sparse spindled cells and inflammatory cells in a sclerotic stroma resembling a scar.[34] Mitotic activity and necrosis are usually absent. The rare and more aggressive epithelioid variant of IMT has plump, round cells with cherry-red nucleoli and abundant inflammation including neutrophils.[35] Immunohistochemistry- Strongly cytoplasmic positivity for vimentin.[36]

Dermatofibrosarcoma protuberans

Dermatofibrosarcoma protuberans (DFSP) is low-grade fibroblastic sarcoma that presents as a dermal or subcutaneous nodule in young adults, usually on the trunk.[37]

DFSP is composed of generally uniform spindle cells. Despite its bland cytology, it infiltrates the dermis and subcutaneous tissue, but does not invade the epidermis. Mitotic figures are not abundant and necrosis is absent, Although DFSP can exhibit evolution to a fibrosarcoma with features of higher grade malignancy.

Immunohistochemistry, the tumor is diffusely positive for the nonspecific marker CD34, reflecting its fibroblastic differentiation.

Malignant

Myxofibrosarcoma

It is a malignant tumor of fibroblastic differentiation that arises in the superficial soft tissue of the extremities, particularly the lower extremities, of older adults.[38] The histologic features of this tumor are variable, but commonly include a multinodular architecture, prominent myxoid stroma, and curvilinear vessels. The tumor is divided into three grades. In low-grade myxofibrosarcoma, overall cellularity and mitotic activity both are low. The nuclei are large and hyperchromatic with cells often containing cytoplasmic vacuoles filled with myxoid material. By comparison, the intermediate-grade tumor is more cellular and has some nuclear pleomorphism. The high-grade forms have sheets or fascicles of markedly pleomorphic cells, including bizarre-appearing multinucleated cells, with abundant mitotic activity and areas of necrosis.

Low-grade fibromyxoid sarcoma

Low-grade fibromyxoid sarcoma is a rare tumor of young to middle aged adults that usually arises in deep soft tissue of the proximal extremities and trunk. Classically, it is a rather hypocellular tumor composed of homogeneous-appearing, hyperchromatic fibroblasts within a collagenized and myxoid stroma. High-grade features, such as nuclear pleomorphism, conspicuous mitotic activity, and necrosis, are absent. Occasionally, tumor cells organize into a rosette-like structure with a central collagenous core.

Immunohistochemistry- typically expresses only vimentin, consistent with fibroblastic differentiation. Myofibroblastic differentiation is reflected by focal smooth muscle actin.[39]

So- called fibrohistiocytictumors

Benign

Benign fibrous histiocytoma

Fibrous histiocytoma is a neoplastic lesion composed of a mixture of fibroblastic and histiocytic cells that are arranged in sheets or short fascicles and are accompanied by varying numbers of inflammatory cells, foam cells and siderophages. Most commonly this tumor occurs in the dermis and superficial subcutis and rarely in deep soft tissues. When located in the skin, fibrous histiocytoma is also referred to as dermatofibroma.

Immunohistochemistry- The combination of factor XIIIa and CD34 is commonly used to distinguish benign fibrous histiocytoma from dermatofibrosarcoma protuberans.[40]

Tenosynovial giant cell tumor

Microscopic appearance of tenosynovial giant cell tumors is variable, depending on the proportions of mononuclear cells, multinucleated giant cells, foamy macrophages, inflammatory cells and haemosiderin, as well as the degree of collagenization of the stroma. Two principal cell types are identified within the mononuclear component: small histiocyte-like cells, with pale cytoplasm and round or reniform nuclei, and larger epithelioid

cells, with amphophilic cytoplasm and round vesicular nuclei. These larger cells often contain a peripheral rim of haemosiderin granules. Most tumors contain a majority of small histiocyte-like cells, but larger cells may predominate. In both types, mitotic activity may be brisk. Necrosis can be seen.

Malignant

Malignant tenosynovial giant cell tumor

Most malignant tenosynovial giant cell tumors are composed of sheets and nodules of enlarged mononuclear cells. These neoplasms tend to show significantly increased mitotic count, including atypical mitosis, necrosis, enlarged nuclei with nucleoli, spindling of mononucleated cells, and myxoid changes. Less commonly, these tumors contain areas resembling undifferentiated pleomorphic sarcoma or myxofibrosarcoma.[41]

Smooth muscle tumors

Benign

Leiomyoma

It occurs in the deep soft tissue or retroperitoneal/abdominal cavity. Leiomyomas of deep soft tissue resemble normal smooth muscle cells because they have eosinophilic cytoplasm and bland, uniform blunt-ended, cigar shaped nuclei. They are arranged in orderly intersecting fascicles.

Immunohistochemistry- tumor cells are always positive for actin, desmin and h-caldesmon. S-100 protein is negative.[42]

Leiomyosarcoma

Leiomyosarcoma is a malignant tumor of smooth muscle that classically arises in the retroperitoneum and proximal extremities with a high rate of local recurrence and metastasis. Microscopically, leiomyosarcoma is ordinarily a highly cellular spindle cell neoplasm in which groups of tumor cells are arranged in intersecting bundles, or fascicles. By H&E stain, the cells display dark, cigar-shaped nuclei and bright pink, or eosinophilic, cytoplasm. Nuclear pleomorphism, mitotic activity, and necrosis are

common findings that are used to distinguish leiomyosarcoma from its benign counterpart leiomyoma. Occasionally, areas of myxoid degeneration are seen.

Immunohistochemitry-Smooth muscle differentiation markers, such as desmin, h-caldesmon, and smooth muscle actin are positive.[43]

Pericytic (perivascular) tumors

Benign and intermediate

Glomus tumornos

Glomus tumors are mesenchymal neoplasms composed of cells that closely resemble the modified smooth muscle cells of the normal glomus body.Typical glomus tumors are subcategorized as “solid glomus tumor”, “glomangioma” and “glomangiomyoma” depending on the relative prominence of glomus cells, vascular structures and smooth muscle bundles respectively.

Glomus cells are small, uniform, rounded cells with a centrally placed, round nucleus and amphophilic cytoplasm. Solid glomus tumors are the most common variant, comprising approximately 75% of cases. They are composed of glomus cells surrounding capillary sized vessels. The stroma may show hyalinization or myxoid change. Small cuffs of glomus cells are often seen around small vessels.

Myopericytoma

Myopericytoma is a benign, generally subcutaneous tumor and is composed of oval to spindle shaped myoid appearing cells with a striking tendency for concentric perivascular growth.

Lesions are composed of relatively monomorphic oval to spindle shaped myoid appearing cells and show striking multilayered concentric growth around lesional blood vessels. The cells have either eosinophilic or amphophilic cytoplasm. Many times, blood vessels outside the lesion also show concentric perivascular proliferation of spindle cells. Lesional blood vessels tend to be numerous and can be variable in size. Subendothelial proliferation of lesional cells in vessel walls is frequently seen. Some

myopericytomas have a component of cells with glomus-type features including cuboidal shape, distinct cell borders, clear to eosinophilic cytoplasm and central round nuclei and the term glomangiopericytoma can be used in such cases.

Immunochemistry- the spindle cells in myopericytomas are positive for smooth muscle actin (SMA).[44]

Angioleiomyoma

A frequently painful, benign subcutaneous or deep dermal tumor composed of mature smooth muscle bundles which surround and intersect between vascular channels.

Angioleiomyomas are subclassified into three subtypes according to the dominant histological pattern: solid, venous and cavernous. Smooth muscle cells of angioleiomyoma are mature and are well differentiated. Mitotic figures are usually absent or rarely seen.

Immunohistochemistry- most cells are positive for alpha smooth muscle actin, desmin, vimentin and collagen type IV and are consistently negative for HMB45.[45]

Malignant

Malignant Glomus tumor

The diagnosis of “malignant glomus tumor” should be reserved for tumors showing:

1) Size >2 cm and subfascial or visceral location; 2) atypical mitotic figures; or 3) marked nuclear atypia and any level of mitotic activity.

Immunohistochemistry- glomus tumors of all types typically express smooth muscle actin and have abundant pericellular type IV collagen production. H-caldesmon is also positive.[46]

Skeletal muscle tumours

Benign

Rhabdomyoma

Rhabdomyoma (RM) is a benign mesenchymal tumor with skeletal muscle differentiation that is classified into cardiac and extracardiac types based

on location. Extracardiac RM is further classified into adult and fetal types, depending on the degree of differentiation. It has a predilection for the head and neck.

Immunohistochemistry- skeletal muscle immunophenotype is demonstrated in all cases, with strong positivity for MSA, myoglobin and desmin.[47]

Malignant

Rhabdomyosarcoma

An aggressive malignancy defined by skeletal muscle differentiation, rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children, but can also occur in adults. RMS arises at any anatomical site, although it is most frequently seen in the head and neck, genitourinary tract, and subfascial tissues of the extremities. Several histologic subtypes of RMS exist with distinct clinical behaviorand prognosis.[48] The current WHO classification recognizes embryonal, alveolar, spindle cell/sclerosing, and pleomorphic subtypes of rhabdomyosarcoma.

Embryonal rhabdomyosarcoma (ERMS) is the most common subtype in young patients, accounting for up to two-thirds of pediatric cases.[49] Histologically, ERMS shows alternating hypercellular and hypocellular, myxoid areas. Mainly tumor cells are primitive appearing, with round, stellate, or spindle cell morphology and hyperchromatic nuclei. More well-differentiated cells with abundant eosinophilic cytoplasm, called rhabdomyoblasts, are found in varying numbers. In their most differentiated form, rhabdomyoblasts produce intracellular myofibrils with cross-striations, so-called “strap cells,” which are seen in about 50% of cases .[48] Botryoid embryonal rhabdomyosarcoma is a rare variant of ERMS occurring at mucosal sites, especially the bladder, vagina, and nasopharynx, with a particularly favorable prognosis. In addition to its typical location, the cells in botryoid ERMS characteristically form a dense “cambium” layer just beneath the epithelium.

The second most frequent subtype of RMS in children, alveolar rhabdomyosarcoma (ARMS), bears a worse prognosis compared to ERMS. Named for its architectural resemblance to lung alveoli, ARMS is composed of nests or sheets of primitive round tumor cells that disperse into single poorly cohesive cells within the center of pseudo-alveoli. Variably thick and interconnecting bands of fibrovascular tissue separate tumor cells. Scattered rhabdomyoblasts are often seen with abundant mitotic activity.

RMS in adults most often takes the form of the pleomorphic or spindle cell variants.[50] These present as atleast intermediate-grade malignancies located in the extremities or trunk wall. Immunohistochemical evidence of expression of master transcriptional regulators of skeletal muscle differentiation (MYOD1 and myogenin) is essential in establishing the diagnosis of adult-type RMS.

Vascular tumors

Benign

Hemangiomas

Venous hemangioma

Venous hemangioma (VH) is composed of veins of variable size, often having thick muscular walls. VH typically consists of large thickwalled vessels, which are variably dilated and commonly display thrombosis with occasional formation of phleboliths. Widely dilated vessels can show attenuation of the walls, mimicking a cavernous hemangioma. Elastic stains reveal the absence of an internal elastic lamina. This helps in the distinction from an arteriovenous hemangioma.

Arteriovenous hemangioma

Arteriovenous hemangioma (AVH) is a non-neoplastic vascular lesion characterized by the presence of arteriovenous shunts. There are two distinctive variants: deep-seated and cutaneous.

When these lesions involve multiple tissue planes, they are termed angiomatosis. This diagnosis always requires clinicopathological and

radiological correlation. AVH is characterized by large numbers of vessels of different sizes, which include veins and arteries with the former largely outnumbering the latter.

Lymphangioma

A benign, cavernous/ cystic vascular lesion composed of dilated lymphatic channels. Cavernous/cystic vascular lymphangiomas are characterized by thin-walled, dilated lymphatic vessels of different sizes, which are lined by a flattened endothelium and frequently surrounded by lymphocytic aggregates. The lumina may be either empty or contain proteinaceous fluid, lymphocytes and sometimes erythrocytes. Larger vessels can have a smooth muscle layer, and longstanding lesions show interstitial fibrosis and stromal inflammation. Stromal mast cells are common and hemosiderin deposition is frequently seen.

Immunohistochemistry- The endothelium demonstrates variable expression of CD31 and CD34.[51]

Intermediate

Kaposi sarcoma

Kaposi sarcoma (KS) is a low-grade vascular neoplasm associated with human herpes virus infection, and is a tumor of the immunocompromised, especially patients with acquiredimmunodeficiency syndrome (AIDS) or iatrogenic immunosuppression secondary to transplantation. In its cutaneous form, KS has 3 distinct clinical stages: patch, plaque, and tumor. In the patch stage, only subtle dermal changes are seen, with increased cellularity around pre-existing vessels and adnexal structures. Proliferating tumor cells occasionally protrude into native vessel lumina, a finding termed the “promontory sign.” Plasma cells are often seen in the background. In the plaque stage, the vascular proliferation becomes much more evident, forming a raised lesion clinically. Proliferative endothelial cells form jagged vessels and at least focally take on a spindle cell morphology. By the tumor stage, a clinical nodule has been formed and the tumor is composed of almost exclusively of monomorphic spindle

cells. Compared to fully malignant angiosarcoma, the neoplastic cells in KS lack pleomorphism and mitotic figures. Several other histologic variants of KS have been described.[52]

Immunohistochemistry-This tumor generally expresses markers of vascular endothelial differentiation i.e.CD31, CD34, and ERG.

Malignant

Epithelioid hemangioendothelioma

Hemangioendotheliomas constitute a family of vascular neoplasms with borderline malignant potential, intermediate between benign hemangiomas and clinically aggressive angiosarcomas. Epithelioid hemangioendothelioma (EHE) is the most aggressive lesion within this family. EHE can occur almost anywhere, including visceral organs, skin, superficial and deep soft tissue, and bone.[53] About half of cases arise from a large vessel, typically a vein. Histologically, EHE is characterized by small nests, cords, and single infiltrating epithelioid endothelial cells present in a chondromyxoid stroma. Classically, scattered tumor cells display intracytoplasmic vacuoles or lumina, some of which harbordegenerated erythrocytes. These so called “blister cells” are pathognomonic of EHE and may represent primitive attempts of vessel formation.

Immunohistochemistry- EHE variably expresses vascular endothelial markers and cytokeratins.

Angiosarcoma

Angiosarcoma is a rare vascular tumor with an aggressive clinical course. It classically occurs in the skin and subcutis of patients with a history of radiation or chronic lymphedema, although cases certainly can arise spontaneously. This lesion has a wide histologic spectrum and, as a result, can be especially challenging to diagnose. On one end, angiosarcomas can mimic a benign hemangioma with only subtle atypical features like nuclear hyperchromasia and infiltrative, asymmetric architecture. Angiosarcomas can be overtly malignant with marked

nuclear atypia, abundant mitotic figures, and sheets of undifferentiated spindle cells or large epithelioid cells, mimicking the morphology of poorly differentiated neoplasms and thus requiring immunohistochemistry to prove endothelial differentiation.

Tumors of peripheral nerves

Benign

Neurofibromas

Neurofibromas may assume one if three growth patterns: localized, diffuse, or plexiform. It is seen most commonly as a superficial, solitary tumor in normal individuals. Diffuse and plexiform neurofibromas are related to neurofibromatosis 1 (NF1).

Histologically, the neurofibroma varies, depending on its content of cells, stromal mucin, and collagen. In the most characteristic form the neurofibroma contains interlacing bundles of elongated cells with wavy, darkly-stained nuclei. The cells are intimately associated with wire-like strands of collagen that have been compared to “shredded carrot”. Small to moderate amounts of mucoid material separate the cells and collagen. The stroma of the tumor is dotted with mast cells, lymphocytes, and rarely xanthoma cells.[54]

Schwannoma (neurilemoma)

Schwannoma (neurilemoma) is an encapsulated neoplasm that most commonly occurs at the flexor surfaces of the extremities, neck, mediastinum, retroperitoneum, posterior spinal roots, and cerebellopontine angle. The nerve of origin often can be demonstrated in the periphery, flattened along the capsule but not penetrating the substance of the tumor. The microscopic appearance is distinctive. Two distinct patterns usually can be recognized, designated by Antoni A and B. the type A areas, which in small tumors comprise almost their entirety, are quite cellular, composed of spindle cells often arranged in a palisading fashion or in an organoid arrangement (verocay bodies). In the type B areas the tumor cells are separated by abundant edematous fluid that may form cystic

spaces. Occasionally, isolated cells with bizarre hyperchromatic nuclei are observed, commonly in so-called *ancient schwannomas.*

Malignant

Malignant peripheral nerve sheath tumor

Malignant peripheral nerve sheath tumor (MPNST) is a high-grade neoplasm that arises from a pre-existing nerve or a benign nerve sheath neoplasm like neurofibroma or less commonly schwannoma. They commonly occur in the proximal extremities of young to middle-aged adults and about half of cases are associated with neurofibromatosis type-I. Histologically, the tumor is composed of malignant spindle cells arranged in alternating hypercellular and hypocellular fascicles. Larger, plump tumor cells tend to aggregate near vessels. Nuclear pleomorphism, mitotic activity, and necrosis are common.

Immunohistochemistry- they are immunopositive for S-100.

Gastrointestinal stromal tumors

Gastrointestinal stromal tumor (GIST) is a mesenchymal neoplasm of the tubular GI tract, particularly the stomach, small bowel, and colorectum, presenting as broad spectrum of clinical behavior from benign to malignant.[55,56] This is a histologically diverse tumor that can have predominantly spindle or epithelioid shaped cells, or a mixture of both. The more common spindle cell variant is characterized by sheets or fascicles of uniform-appearing cells with cigar shaped nuclei and pale pink cytoplasm. The cells can arrange palisading manner with vacuoles often seen around nuclei, especially in gastric GISTs. Haphazard packets of coarse collagen fibers, called skeinoid fibers, are seen with some bias for GIST arising in small bowel. By contrast, the less common epithelioid variant has larger round uniform cells, having clear to eosinophilic cytoplasm and occasional perinuclear vacuoles. GISTs are believed to originate from the interstitial cell of Cajal, the pacemaker of the autonomic motor system of the GI tract.[57] There are established criteria to predict malignant potential of GISTs, which can help guide therapeutic decision

making. This risk stratification system takes into account mitotic activity, tumor size, and anatomical origin.[58]

Immunohistochemistry- Expression of KIT (CD117) or DOG-1 (discovered on GIST) is of diagnostic value.[59]

Tumors of uncertain differentiation

Benign

Myxoma

It is a benign soft tissue tumor characterized by bland spindle shaped cells embedded in hypovascular and myxoid stroma.

Grossly, the tumors have a gelatinous, lobulated cut surface. The classic intramuscular myxoma is composed of uniform and cytologically bland spindle and stellate shaped cells with tapering eosinophilic cytoplasm and small nuclei. The cells are separated by abundant myxoid extracellular stroma containing very sparse capillary sized vessels. Sections from the interface of the tumor and the surrounding skeletal muscle frequently show infiltration between muscle fibres or around individual skeletal muscle cells, which may be atrophic.

Immunohistochemistry- The cells stain for vimentin and show variable staining for CD34, desmin and actin. There is no staining for S100 protein.[60]

Aggressive angiomyxoma

A soft tissue neoplasm with a predilection for pelvic and perineal regions and its tendency for local recurrence. It is composed of small stellate and spindle cells in a myxoedematous stroma with entrapped regional structures. The tumors are of low to moderate cellularity and are composed of relatively uniform, small, stellate and spindled cells, set in a loosely collagenous, myxoedematous matrix with scattered vessels of varying sizes and entrapped regional structures. The tumor cells have scant, pale, eosinophilic cytoplasm with poorly defined borders and relatively bland nuclei with an open chromatin pattern and a single, small centrally located nucleolus. A characteristic finding which seen in most

cases is the presence of loosely organized islands of well-developed myoid cells around the large nerve segments and vessels.

Immunohistochemistry- the tumor cells of angiomyxoma usually show diffuse immunoreactivity for vimentin, moderate to diffuse (nuclear) immunoreactivity for estrogen and progesterone receptor protein, and variable levels of immunoreactivity for actins and CD34. Desmin positivity can be identified in almost all cases.[61]

Malignant

Synovial sarcoma

Named for its vague morphologic resemblance to synovium, synovial sarcoma (SS) is a high-grade malignancy that most commonly arises in the extremities of young adults, but can affect patients of any age at essentially any anatomical site.[62] Despite its name, this tumor is not derived from synovium and its cell of origin remains unclear. Histologically, the tumor is highly cellular and shows 1 out of 2 major patterns. In the “monophasic” form, the cells are uniformly spindled (oval to cigar shaped), or less commonly, epithelioid (polygonal cells with distinct cytoplasm). In the “biphasic” form, both spindled and epithelioid elements co-exist, the latter of which can form glandular structures reminiscent of epithelial neoplasms. Large gaping blood vessels are seen in the background.

Immunohistochemistry- the tumor cells usually express cytokeratins (especially in epithelioid areas) and, more specifically, the transcriptional co-repressor TLE1.[63]

Ewing sarcoma

It is the “small round blue cell tumor”. This high-grade malignancy is the second most common bone and soft tissue sarcoma in children. As the name suggests, the tumor is composed of sheets of undifferentiated tumor cells with dark, round nuclei, and scanty cytoplasm. Two entities previously thought to be biologically distinct and now considered variants of ES are peripheral primitive neuroectodermal tumors and Askin tumor. Peripheral primitive neuroectodermal tumor differs from classic ES only in

that it has peculiar wreath-like arrangements of cells termed Homer-Wright rosettes that may represent some degree of neural differentiation. The Askin tumor is simply ewing sarcoma that distinctively arises in the chest wall of adolescents.[64]

Desmoplastic small round cell tumor

It is a highly aggressive, treatment-resistant sarcoma typically arising in the abdomen of young men. Histologically, the tumor is composed of nest or sheets of undifferentiated small cells set within a prominent desmoplastic or fibrous stroma. The cells are mitotically active, and areas of central tumor necrosis are common.

Immunohistochemistry - WT1 is positive in most cases.[65]

FNCLCC grading

Definition of parameters

Differentiation

Score 1:Sarcoma closely resembling normal adult mesenchymal tissue (e.g., well-differentiated liposarcoma)

Score 2:

Sarcomas for which histologic typing is certain (e.g., myxoid liposarcoma)

Score 3:

Embryonal and undifferentiated sarcomas, sarcomas of doubtful type, and synovial sarcomas.

Mitotic Count

Score 1: 0–9 mitoses per 10 HPF

Score 2: 10–19 mitoses per 10 HPF

Score 3: ≥20 mitoses per 10 HPF

Tumor Necrosis

Score 0: No necrosis

Score 1: <50% tumor necrosis

Score 2: ≥50% tumor necrosis

Grading:

- **Grade 1:** total score of 2 - 3 points
- **Grade 2:** total score of 4 - 5 points
- **Grade 3:** total score of 6 - 8 points

Grade particularly indicates the probability of distant metastasis and overall survival, but is of poor value for predicting local recurrence which is mainly related to the quality of surgical margins.

LIMITATIONS OF HISTOLOGICAL GRADING

The weakest component of FNCLCC grading system is the differentiation component, which is relatively subjective and can be difficult to assess if there is no normal tissue counterpart for comparison, such as in the case of undifferentiated pleomorphic sarcoma. Furthermore, STS grading systems have been developed based on the entire heterogeneous STS population and may not be generalizable to every histological subtype; indeed, some histotypes define the dominant clinical behavior and therefore histotyping is more important than grading in these cases. For example, atypical lipomatous tumor/well-differentiated liposarcoma, dermatofibrosarcoma protuberans,Infantile fibrosarcoma and angiomatoid fibrous histiocytoma are Grade 1; Ewing sarcoma/PNET, rhabdomyosarcoma (except spindle celland botryoid variants), angiosarcoma, pleomorphic liposarcoma, soft tissue osteosarcoma, mesenchymal chondrosarcoma, desmoplastic small round cell tumor, and extra-renal malignant rhabdoid tumor are Grade 3; and alveolar soft part sarcoma, clear cell sarcoma, and epithelioid sarcoma are not graded but are usually considered high-grade for management purposes.[66]

Ancillary testing in soft tissue tumors

Ancillary testing of surgical pathology specimens began soon after the birth of histopathology. A variety of histochemical stains became available, and these were supplemented by a variety of techniques designed to show microbial organisms or specialized cells. With soft tissue tumors, periodic acid–Schiff (PAS) stains were routinely used until the 1990s to detect the abundant glycogen associated with Ewing sarcoma or the

crystals associated with alveolar soft part sarcoma. Phosphotungstic acid–hematoxylin staining was used to highlight the cross-striations associated with myogenic differentiation in rhabdomyosarcomas. This search for methods to delineate cytologic detail and characteristic tissue structure eventually led to immunohistochemistry

(IHC), which added immunological techniques to chemically based stains.[67] Electron microscopy (EM) was first invented as a technique in the 1940s[68] for observing subcellular detail in cells. When it became apparent that fine cellular detail of tumors could be discerned,[69] then EM became adapted for surgical pathology in general and tumor diagnosis in particular. The appearance, morphology, and topical distribution of submicroscopic organelles correlated with specific tissue types, which in turn were the basis of tumor diagnosis and classification.[70] In this manner, features such as myosin and actin filament bundles and Z-bands were searched for with rhabdomyosarcomas, and neurosecretory granules were detected in peripheral neuroectodermal tumors. Some structures, such as the crystalline organelles seen in alveolar soft part sarcoma,[71] became characteristic features of a diagnosis, even if determination of the cell type proved elusive. This method continues to be used as an ancillary technique for tumor diagnosis, but it has lost some of its luster due to the lower cost, widespread availability, and relative ease of IHC.

Role of IHC

Introduced in the early 1980s, immunohistochemistry is now a standard tool for evaluating the diagnosis and prognosis of tumors.[72]

After~30 years of widespread usage, immunohistochemistry (IHC) has become a standard method of diagnosis for surgical pathology. It is a method to identify specific antigen within a tissue section utilizing an antigen specific antibody. Detection at the light microscopic level of antigen antibody interaction can be achieved by labelling the antibody with a substance that can be visualized, which can be done either by

conjugation to fluorescent marker or enzyme followed by the calorimetric detection.

Because of the diversity of diagnosis and often subtle nature of diagnostic criteria, IHC finds particular utility in soft tissue tumors. The use of progressively small amounts of tissue for diagnosis highlights the importance of this method. The sensitivity and crispness of IHC stains have progressively improved with the advent of new techniques. Traditionally, IHC detects cell-typic markers that characterize cell phenotypes, such as chromogranin for neuroectodermal tissue, myogenin for skeletal muscle, and cytokeratin for epithelium. It is used to detect tumor-specific alterations which add significantly to histological interpretation.

However, the advent of genetic discoveries have led to IHC testing for detection of fusion gene products or overexpressed oncogenes associated with deletions and mutations. Immunohistochemistry (IHC) technique is widely used in diagnostics and research, and its applications continue to be extended because of its ease of use, reliability, and versatility.

The initial approach of most tumor diagnosis with IHC application is distinguishing mesenchymal from epithelial differentiation using markers vimentin and cytokeratin. IHC provides a relatively rapid and simple method to determine the origin of neoplastic tissue or investigate the behavior or progression of a given neoplasm.

The use of positive and negative controls is paramount and should be employed in routine IHC. Negative control confirms that the staining being reported is due to the antibody binding, and positive control confirms that the antibody is working and that the suspected target of the antibody is the actual target. Internal controls, normal tissues on the stained slide known to be either positive or negative for the marker in question, are excellent confirmatory evidence. [73] Immunohistochemical markers are monoclonal antibodies used to identify specific protein in a tissue section. The antibody binds to the protein being assessed and a color reagent stains

the protein, if that protein is present in the tissue. So identification of differentiation proteins is required for tumors that cannot be readily classified on routine sections alone.[74]

The first immunohistochemistry procedure was performed in 1941 when Coons et al used a fluorescent antibody to detect bacteria in tissue. This success led to the development of similar tests which helped in the diagnosis of autoimmune disease. By the 1960s, many research laboratories made and used these fluorescent antibodies to detect a number of tissue antigens. Earlier procedures were applied only to unfixed, frozen tissue, rather than fixed tissue, resulting in poor morphology and a slide that could not be easily archived. These drawbacks, combined with interference by tissue auto fluorescence, fading of the fluorescent label led to the pursuit of new methods. Investigators tried to label antibodies by using metal-storage proteins such as ferritin and enzymes such as acid phosphatase.[75]

In 1960 Nakano and Pierce succeeded in labeling an antibody with horseradish peroxidase, which is an inexpensive and readily available enzyme that could be easily detected with the permanent substrate 3,3-diaminobenzidine (DAB). In 1970, Sternberger and colleagues used an enzymatic histochemical method to detect antibody using peroxidase antiperoxidase (PAP) and DAB. In this procedure, the primary antibody was not labeled with horseradish peroxidase. This method called for inserting the secondary antibody after the primary one, then adding PAP and DAB substrate. The end product of this reaction was a brown precipitate that could be seen under a bright-field microscope. This approach was known as the PAP technique. With the publication of the this technique came a race to better understand and take advantage of immunohistochemistry technology.By the 1990s, however, the potential use of immunohistochemistry in surgical pathology became apparent, but the focus shifted to applying immunohistochemistry to formalin-fixed tissues.

Huang and his co-workers used a proteolytic enzyme (trypsin) to make available antigen sites that were masked by the fixative. Although their work involved indirect immunofluorescence methods. With this enzymes such as trypsin, pepsin and protease became a common adjunct to fixed-tissue immunohistochemistry.In the late 1990s, Guesdon and his colleagues, studied the effects of covalently labeling enzymes, antigens, and antibodies with biotin. They developed the bridge avidin-biotin and the labeled avidin-biotin techniques for detecting antibodies by enzyme immunoassay and enzyme-immunohistochemical staining. The enzymes which were used in labeling experiments included peroxidase, alkaline phosphatase, glucose oxidase, and 3-galactosidase. These sensitive and reproducible methods formed the basis of methods still in use, such as those in the avidin-biotin and labeled streptavidin kits.[76]

The immunohistochemistry technique is used in the search for cell or tissue antigens ranging from amino acids and proteins to infectious agents and specific cellular populations. The technique comprises of two steps:

A: slide preparation (specimen fixation and tissue processing) and stages evolved for the reaction (in order: antigen retrieval, non-specific site block endogenous peroxidase block, primary antibody incubation, and the employment of systems of detection, revealing and counterstaining and also slide mounting and storage)

B: interpretation and quantification of the obtained expression.[77]

Basic panel of antibodies: An initial panel of antibodies is often required in order establish the broad lineage. The initial panel for suspected mesenchymal tumor includes S100, Desmin, cytokeratin, EMA, SMA, Vimentin, CD34.

CD34

CD34 is a transmembrane glycoprotein containing sialomucin elements. It is believed to be important in the regulation of cell recognition and trafficking. CD 34 was originally recognized as an antigen expressed in hematopoietic stem cells, and remains one of the key markers in their

characterization.[78] As a membrane antigen, CD34 is expressed typically in a distinct membrane pattern, which is more obvious in cells with epithelioid morphology. CD34 is expressed in vascular endothelial cells, but often shows a weaker expression in lymphatic endothelia. Originally reported specifically in periadnexal and perivascular dermal fibroblasts,[79] CD34 is also expressed in other soft tissue fibroblasts and septal and stromal elements in various visceral locations. CD34 is a multispecific marker, which is nevertheless highly useful in soft tissue tumors. CD34 is a marker of many types of fibroblastic tumors, such as dermatofibrosarcoma protuberans,[80] contrasting with dermatofibroma/benign cutaneous fibrous histiocytoma.[81] Solitary fibrous tumor is also CD34-positive [82] but, similar to dermatofibrosarcoma, the corresponding fibrosarcomatous or 'de-differentiated' forms may show low or no expression. A variety of other, mostly morphologically highly distinctive fibroblastic tumors, are also CD34- positive, so that CD34-positivity alone does not define any fibroblastic tumor type. Among these are the benign superficial acral fibromyxoma,[83] and malignant tumors such as myxofibrosarcoma and de-differentiated liposarcoma, which are variably positive. CD34 is expressed in many lipomatous tumors, and particularly strongly in the spindle cell component in spindle cell and pleomorphic lipoma.[84] In vascular endothelial tumors, CD34 highlights the endothelial component of benign angiomas. Its expression is variable (50–60%) in malignant endothelial neoplasms, such as epithelioid haemangioendothelioma and angiosarcoma; however, CD34 is expressed consistently in Kaposi sarcoma.[78] Approximately 50% of epithelioid sarcomas show membranous positivity for CD34, whereas positivity in carcinomas and other epithelial or keratin-positive neoplasms, such as synovial sarcoma, is very rare.[85]

Desmin

Desmin is the intermediate (10 nm diameter) filament protein of muscle cells and is expressed typically in skeletal muscle and most smooth

muscle cells, except some vascular smooth muscle. When judging desmin positivity in tumors, its presence in entrapped reactive smooth or skeletal muscle cells must be carefully excluded. A commonly used clone is D33, with excellent performance in formalin-fixed tissue following heat-induced epitope retrieval. Desmin is also expressed in a subset of interstitial reticulum cells of lymph nodes and the so-called myoid cells in thymus. Desmin is useful in the diagnosis of skeletal muscle and smooth muscle tumors. In some cases, desmin immunohistochemistry can appropriately alert one to an unusual rhabdomyosarcoma, which has to be evaluated further with additional, more lineage-specific markers such as myogenin and MyoD1. Similarly, h-caldesmon is another useful marker to support smooth muscle differentiation. Desmin can also be present in myofibroblasts, and therefore myofibroblastic tumors such as desmoid fibromatosis can be focally positive.[86] Notably, desmin is expressed strongly in a number other tumors, none of which can be considered skeletal or smooth muscle tumors. The most important examples include desmoplastic small round cell tumor, which often contains desmin positive perinuclear dots.[87,88] Even Ewing sarcoma can be occasionally desmin-positive. In aggressive angiomyxoma, desmin immunostain highlights the cytoplasm of dendritic-shaped tumor cells, as well as possible perivascular smooth muscle elements.[89] Cellular angiofibroma in the pelvic/inguinal region is variably desmin positive, and approximately half of angiomatoid fibrous histiocytomas contain desmin positive tumor cells.[90,91] Tenosynovial giant cell tumors often contain scattered desmin-positive dendrite-shaped cells, which can help to identify these tumors when seen at unusual locations.[92]

Alpha smooth muscle actin (SMA)

While all cells contain actin microfilaments as part of their cytoskeleton, SMA has some specificity for smooth muscle cells. It is also expressed in the smooth muscle-related pericytes and glomus cells, and in myofibroblasts and myoepithelial cells. SMA can be utilized as marker to

diagnose myofibroblastic, smooth muscle and related tumors. In order to observe the true tumor cell phenotype, one has to distinguish reactivity in tumorcells from that in entrapped non-neoplastic cells, and this can be tricky at times. Among the myofibroblastic tumors, nodular fasciitis and fibroma of tendon sheath are strongly positive, a fact that should not lead to confusion with smooth muscle tumors, such as leiomyosarcoma. SMA is expressed in 30% of GISTs, so that othermarkers such as KIT also have to be used. In addition, SMA can be applied in detection of pericytic cell populations in vascular tumors and myoepithelial cell differentiation in neoplasms. However, in soft tissue myoepithelioma this is rarely fruitful.[93]

S100 protein

S100 protein, so named based on its 100% solubility to neutral ammonium sulphate, was isolated originally from brain tissue and subsequently shown to be a good marker for Schwann cells, melanocytes, glial cells and some neurones of the brain. In addition, S100 protein is also expressed in cutaneous Langerhans cells, their derivatives interdigitating reticulum cells of lymphoid tissue, adipocytes, cartilage and some myoepithelial cells.[93,94] Although S100 protein is actually encoded by a multigene family with various subunits, polyclonal multispecific antibodies are typically used and analysis with subunit-specific antibodies is not widely used in clinical practice. Despite its multispecificity, S100 protein is a very useful marker in the evaluation of soft tissue tumors. Polyclonal antibodies are still the most commonly used, often with no epitope retrieval. The polyclonal antibody requires careful titration of the dilution to obtain the maximal possible detection sensitivity and specificity. S100-positive dendritic antigen-presenting cells are a ubiquitous internal control, especially useful when evaluating tumors. S100 protein is useful in detecting Schwann cell differentiation in nerve sheath tumors and highlighting normal Langerhans cells in skin and interdigitating reticulum cells in lymphoid tissue, as well as Langerhans cell histiocytosis and related lesions, and also the large histiocyte-like cells typical of Rosai–Dorfman disease. Metastatic

melanoma is typically strongly positive for S100 protein and is perhaps the most common S100-positive malignant soft tissue tumor. In fact, malignant peripheral nerve sheath tumors (MPNST) are more commonly S100 protein-negative than positive, although they may contain S100 protein-positive residual Schwann cells of the pre-existing neurofibroma. S100 protein-only phenotype of metastatic melanoma (without more melanoma-specific markers such as HMB45 and MelanA) may be difficult to differentiate from S100 protein-positive MPNST. Nodal tumor location and the history of melanoma would point towards metastatic melanoma, although it should be remembered that the melanoma-related clear cell sarcoma of soft parts may also metastasize to lymph nodes; the distinction of melanoma from clear cell sarcoma is aided by genetics, as the latter contains EWSR1 gene rearrangements, in contrast to melanoma. The pre-existing neurofibroma component within the tumor is practically the only definitive evidence for MPNST over other neuroectodermal malignancy. In some cases, the distinction may be impossible and then the descriptive diagnosis of 'malignant neuroectodermal neoplasm' (including melanoma, MPNST and possibly also clear cell sarcoma) is appropriate. S100 protein is also expressed in cartilage cells and has some value in identification of cartilaginous components in various tumors. It may also be useful in pin pointing atypical adipocytes and lipoblasts in the diagnosis of atypical lipomatous tumors and liposarcomas. The SOX10 transcription factor is emerging as a new marker for schwannian and melanocytic tumors, although the data are still somewhat limited.[95]

KIT (CD117)

KIT receptor tyrosine kinase is a key cell signaling molecule, also referred to as CD117. It becomes normally activated (phosphorylated) when binding of its ligand stem cell factor links together two KIT molecules which then cross-phosphorylate each other's KIT tyrosine kinase domain, making it ready to phosphorylate downstream targets in the KIT signal transduction cascade. Activation of the KIT signaling pathway typically

promotes cellular growth over apoptosis. A classical example of pathological KIT activation by gain-of-function mutation occurs in GISTs, most of which have these mutations.[96-100] KIT-dependent and immunohistochemically KIT-expressing cells include hematopoietic stem cells, mast cells, germ cells, melanocytes, certain epithelia (especially in skin adnexa) and Cajal cells of the gastrointestinal tract.[101,102] The main application of KIT detection by immunohistochemistry is identification of GIST, but rare subsets of other soft tissue tumors can be positive. These include Ewing sarcoma and angiosarcoma, and extra skeletal myxoid chondrosarcoma has also been reported to be occasionally positive. Neovascular endothelia in various tumors can also be KIT-positive, which should not be confused with tumor cell immunophenotypes.[103,104] The search for treatment targets for KIT inhibitors by immunohistochemical KIT-positivity only is no longer considered a valid idea. GIST always needs to be recognized specifically, as these tumors can have specific oncological treatment with KIT–tyrosine kinase inhibitors such imatinib and the expanding family of newer inhibitors. GIST has to be included in the differential diagnosis not only for gastrointestinal but also for any intraabdominal or hepatic mesenchymal tumors. In our experience, GISTs are more common than true leiomyosarcomas in the retroperitoneum. Furthermore, rare peripheral soft tissue or skin metastases can be diagnostic pitfalls. The most practical way to evaluate GIST is immunohistochemistry for KIT, which captures >95% of GISTs. A small subset of GIST that especially include some PDGFRA mutant gastric GISTs can be KIT-negative or only focally positive. However, these GISTs are typically positive for DOG1/Ano-1.

DOG1/ANO-1

DOG1 (discovered on GIST), also known as Anoctamin-1 (Ano-1) is a calcium-activated chloride channel protein expressed strongly in the gastrointestinal Cajal cells and GISTs. This gene product was named following discovery in GIST in expression arrays, and was also discovered

independently and alternatively named as a transmembrane protein 16A (TMEM16A), overexpressed in oral (squamous cell) carcinoma 2 (ORAOV2) and tumor-amplified and overexpressed sequence1 (TAOS1).[105-107] DOG1/Ano-1 has been recognized as a valuable alternative marker after KIT. It is especially useful in KIT-negative gastric GISTs, many of which are PDGFRA-mutant tumors: such mutants still appear strongly positive for DOG1.[108,109] Relatively few non-GIST mesenchymal tumors are positive for DOG1. Such tumors include a minority of benign and malignant smooth muscle tumors and synovial sarcomas (DOG1 positivity in all these categories is rare). In addition, endothelial cell labelling is also possible. However, DOG1 is expressed commonly in gastrointestinal carcinomas, especially esophageal squamous cell carcinomas and various adenocarcinomas. Normal gastric mucosa can also be positive.[110,111]

MDM2 AND CDK4

The MDM2 gene and its neighboring gene CDK4 are amplified in atypical lipomatous tumors, which can be detected by molecular methods such as reverse transcription–polymerase chain reaction (RT-PCR) and FISH. The resultant MDM2 and CDK4 protein overexpression can be detected by IHC. However, nuclear staining with MDM2 and CDK4 is not entirely specific for atypical lipomatous tumor. For example, MDM2 or CDK4 can show positivity in intimal sarcoma, pleomorphic rhabdomyosarcoma, a subset of malignant peripheral nerve sheath tumor, and myxofibrosarcoma.[112-116] Meanwhile, these markers are useful to distinguish atypical lipomatous tumor from lipoma as well as dedifferentiated liposarcoma from undifferentiated sarcoma, especially when both markers show positivity. Pleomorphic liposarcoma and myxoid liposarcoma are negative for MDM2 and CDK4.[117]

Keratins

Keratins are a complex family of cytoskeletal intermediate filament proteins expressed typically in various epithelia in a differentiation

dependent manner. Diagnostically more important in soft tissue tumors are simple epithelial (‘low molecular weight’) keratins, based on their wider expression profile in different epithelial cells. However, on balance, these keratins may have increased presence in mesenchymal cells so that careful judgement and possibly additional markers are needed to determine whether or not their expression signifies epithelial differentiation. Keratin proteins present in regular epithelia (‘soft keratins’) are encoded by two multigene families, with the individual names abbreviated as KRT, followed by a number. The classic keratin catalogue of Moll et al. classifies denatured and urea-depolymerized keratins by molecular masses and isoelectric points by two-dimensional gel electrophoresis.[118] Type 2 (or B for basic) keratins with more basic isoelectric points are numbered 1–8 from the highest to lowest molecular weight. Of these, numbers 7 and 8 are more important in soft tissue tumors. Type 1 (or A for acidic) keratins have lower (more acidic) isoelectric points and are numbered 9–18, from the highest to lowest molecular weight. Keratin 20, a later addition to the Moll et al. catalogue, also belongs to this family. Most important in soft tissue tumors are lower molecular weight keratins of this group, keratins 18 and 19.[118-120] Although type-specific antibodies are available for nearly all individual keratins, multispecific keratin antibodies such as AE1 (recognizing keratins 9–17) and AE3 (recognizing keratins 1–8) have wide practical use, often as a cocktail containing both antibodies. Note that even the AE1/AE3 cocktail does not detect all keratins, and in particular has a ‘blind spot’ in not recognizing keratin 18. Therefore, alternative multispecific or K18-specific antibodies have to be used to detect keratin 18. The lower molecular weight keratins (7, 8, 18 and 19) are expressed generally in non-stratified (simple epithelia), and the higher molecular weight keratins (5, 6, 13, 14) are present in stratified epithelia andbasal cells of complex glandular epithelia (such as respiratory epithelia). Selective mesenchymal expression of keratins includes the presence of keratins 7, 8 and 18 in

some smooth muscle cells (myometrium, vascular and some parenchymal smooth muscle) and expression of keratins 7 and 18 in some vascular endothelial cells.[120] Keratin 20 has a very characteristic distribution, being present in intestinal epithelia, the uppermost layer of urothelia (the umbrella cells) and in Merkel cells. In soft tissue tumors, K20 is practically important as a marker for Merkel cell carcinoma.[121,122] Soft tissue tumors with epithelial differentiation include synovial sarcoma and epithelioid sarcoma, and these tumors generally express simple epithelial keratins K8, K18 and K19. In addition, keratin 7 is also expressed in synovial sarcoma but usually not in epithelioid sarcoma. Even the high molecular weight keratins typical of stratified epithelia and keratin 20 can be focally present in biphasic synovial sarcoma.[123] Mixed tumors or myoepitheliomas of soft tissue most commonly contain keratin-positive elements, as detected with the AE1/AE3 keratin cocktail, but keratin subtypes have not been analyzed in detail.[124] As might be expected from normal tissue distribution, keratins (especially K7 and K18) are also present in some vascular endothelial neoplasms (especially hemangiomas and some angiosarcomas) and in some smooth muscle tumors. In addition, K8 is expressed in some angiosarcomas.[125,126] Additional sarcomas with keratin expression include desmoplastic small round cell tumor (typically extensive) and Ewing sarcoma (almost always focal, if present). Experimental studies showed that virally transformed cultured fibroblasts can also express keratins, especially K8 and K18, and this forms a logical scientific basis for the observation that various sarcomas with non-epithelial differentiation can also show variable, usually limited keratin expression.[127,128] For example, myxofibrosarcomas and related tumors somewhat frequently contain keratin-positive tumor cells. A specific problem related to AE3 antibody is cross-reactivity in the brain, possibly via its cross-reaction with GFAP.[129] This may be the reason why schwannomas (especially spinal and retroperitoneal lesions) can also be AE1/AE3-positive.[130]

CD31

Also known as PECAM-1 (platelet-endothelial cell adhesion molecule-1), CD31 is a cell membrane protein expressed in endothelial cells, platelets and some primitive hematopoietic (myeloid) cells.[131] CD31 has been the gold standard as a marker for endothelial differentiation in the recognition of vascular endothelial tumors. Although benign angiomas can usually be diagnosed histologically, the diagnosis of malignant vascular tumors – epithelioid hemangioendothelioma, angiosarcomas and Kaposi sarcoma – is aided by demonstration of CD31, which is expressed almost universally in this group.[132-134] The use of additional endothelial markers such as ERG is beneficial as a double confirmation for any malignant endothelial tumor, especially in poorly differentiated tumors. HHV-8 offers a specific confirmation for Kaposi sarcoma. In addition, CD31 is expressed in some other mature hematopoietic cells, especially some plasma cells and histiocytes. The latter-mentioned immunoreactivities are pitfalls in diagnostic use, potentially causing overdiagnosis of endothelial differentiation.[135]

Epithelial membrane antigen(EMA)

EMA is a glycoprotein also known as MUC1 apoprotein. It is expressed in a variety of ductal, secretory and other epithelial cells, often in a luminal membrane pattern. In addition, EMA is expressed in meningothelial and perineurial cell membranes and in subpopulations of plasma cells. The monoclonal antibody clone E29 is used commonly to detect EMA in routinely processed tissue, and performs well following heat-induced epitope retrieval.[136] EMA is useful in detecting epithelial differentiation in soft tissue tumors, and in such tumors it is typically detectable in synovial sarcoma, epithelioid sarcoma, myoepithelioma and many, but not all, metastatic carcinomas. Notably, some other sarcomas, such as leiomyosarcoma and rarely angiosarcomas, can also be positive, and this has to be considered in the differential diagnosis. EMA is also useful in the diagnosis of meningiomas and perineuriomas, most of which show at least

focal positivity.[137,138] Specific variants of perineuriomas have been discovered based on EMA positivity, supplementary perineurial cell markers (claudin-1, GLUT-1) or ultrastructural analysis. Among these variants are sclerosing perineurioma of fingers [139] and spindle cell perineuriomas of soft tissue in general.[140-142] Most perineuriomas are identified on the basis of slender or slightly epithelioid spindle cells in lamellar organization showing variable positivity for EMA. It is not known whether EMA positivity, often detected in low-grade fibromyxoid sarcoma,[143] is due to real expression of MUC1 or possible cross-reaction of the MUC1 antibodies with MUC4, another EMA-family protein, which is expressed highly in low-grade fibromyxoid sarcoma.[144]

Vimentin

Vimentin is a type II intermediate filament protein encoded by the VIM gene. Vimentin is expressed in mesenchymal cells but is not specific for mesenchymal cells. It is also expressed in certain types of carcinomas (e.g., renal cell carcinoma, spindle cell carcinoma), as well as lymphomas and melanomas. Vimentin positivity has a limited value in the diagnosis of soft tissue tumors; however, if the mesenchymal tissue is negative for vimentin, it may indicate that the tissue is suboptimal for IHC or not of a mesenchymal (soft tissue) differentiation.

h- caldesmon

Alpha-smooth muscle actin (SMA) is one of the most specific markers of smooth muscle cells (SMC), and it has been widely used to distinguish the tumors from non-muscle tumors. [145,146] However, because myofibroblasts also express SMA, [146,147] it is sometimes difficult to differentiate LM and LMS from tumors with myofibroblastic differentiation. Caldesmon (CD) is a protein widely distributed in both smooth and non-smooth muscle cells.[148-153] It combines with calmodulin, tropomyposin, and actin and is thought to regulate cellular contraction.[149] There are two isoforms, high-molecular-weight (h-caldesmon; h-CD) and low-molecular-weight (l-caldesmon; l-CD) types,[149,150] and h-CD has been reported to be specific for SMC.[150,154]

The former is present in many kinds of cells, and the latter is exclusively present in vascular and visceral SMC.[150,154], The content of h-CD in aortic SMC is rather low in the fetus and newborn, compared with that of adult aortic SMC, and it increases gradually during several months of postnatal growth. Conversely, the content of SMA in the fetus at 24 weeks of gestation is close to that of adult.[152] These observations indicate that h-CD is specifically expressed in the matured SMC. Non-neoplastic myofibroblasts did notshow reactivity for h-CD in previous immunohistochemical studies.[154] h-Caldesmon appear to be relatively specific for smooth muscle differentiation and, as such, are useful adjuncts to desmin and actin immunostains in the evaluation of leiomyoma and LMS.[155,156] The vast majority of leiomyomas express h-caldesmon, but expression in LMS is more variable, with one study showing reactivity for h-caldesmon in only 36% of LMS.[157] Caldesmon expression is not entirely specific to smooth muscle tumors, however, because reactivity is also observed in the majority of gastrointestinal stromal tumors (GISTs), glomus tumors, and myopericytomas.[158,159] In contrast, myofibroblastic cells do not express caldesmon.[160,161]

Proliferation-based markers such as Ki-67 can also be used for prognosis and grading, but more standardization is needed. In the same vein, it is emphasized that immuno- histochemical (IHC) evaluation of mesenchymal neoplasms is merely an adjunct to thorough histologic evaluation, not a substitute for it as only histomorphological diagnosis is going to help us to choose from wide variety of markers available based on histological pattern of the tumor.

In a retrospective study done in1995 ***by kransdorf et al,*** More than 80% of malignant tumors were classified into eight diagnostic categories: malignant fibrous histiocytoma (24%), liposarcoma (14%), leiomyosarcoma (8%), malignant schwannoma (6%), dermatofibrosarcoma protuberans (6%), synovial sarcoma (5%), fibrosarcoma (5%), and sarcoma, not classified further (12%).

Approximately 79% of all malignant tumors were classified into five diagnoses for each age and location. With the distal upper extremity (hand and wrist) as an example, 50% of malignant lesions in the 16-25 yearold group were classified as epithelioid sarcoma (29%), malignant fibrous histiocytoma (13%), and synovial sarcoma (8%). For the same location but for children 5 years old or younger, almost 50% of malignant tumors were classified as infantile fibrosarcoma.[162]

Andrew et al in 2000 studied "Immunohistochemical Detection of FLI-1 Protein Expression" in 132 cases of round cell tumors.They studied 132 cases of pediatric and adult small blue round cell tumor, including 41 ES/PNET, 32 rhabdomyosarcoma, 30 neuroblastoma, 8 poorly differentiated synovial sarcoma, 8 ethesioneuroblastoma, 8 lymphoblastic lymphoma, 3 wilm's tumor, 1 desmoplastic round cell tumor, and 1 mesenchymal chondrosarcoma. They demonstrated FLI-1 protein expression in over 70% of ES/PNET with a specificity of over 90%. These findings strongly suggest that antibodies to FLI-1 may play a valuable adjunctive role in the diagnosis of ES/PNET.[163]

Manuela et al in 2002 studied immunohistochemical findings in 60 cases of monophasic and poorly differentiated synovial sarcoma and found that Ninety-eight percent of SS were focally or diffusely positive for, at least, one epithelial marker (i.e., EMA, cytokeratin AE1/AE3, cytokeratin KL1, and/or E-cadherin).One case of PDSS, was consistently negative for all these markers. MFSS and PDSS were positive for EMA in 100% and 92% of the cases, respectively. In the MFSS category, 70% of the cases were positive for cytokeratin AE1/AE3, 49% for cytokeratin KL1, and 47% for E-cadherin. In PDSS, 46% of the cases were positive for cytokeratin AE1/AE3, 38% for cytokeratin KL1, and 54% for E-cadherin, at least focally. CD34 was focally positive in three MFSS and negative in all PDSS. They suggested that reactivity for EMA, cytokeratin AE1/AE3, and E-cadherin, in combination with CD34 negativity, are the most useful and sensitive markers for diagnosing SS.[164]

In a retrospective study done by ***Jean michelcoindre et al*** in 2003, 12 cases of inflammatory MFH and 8 cases of dedifferentiated liposarcomas that had an inflammatory MFH were included. Immunohistochemistry showed positivity of tumor cells for MDM2 in every tumor in both groups and for CDK4 in ten and seven inflammatory MFHs and dedifferentiated liposarcomas, respectively. They concluded, extensive sampling, particularly in the adipose areas, should be performed in order to demonstrate a well-differentiated liposarcoma component. Demonstration of MDM2 and CDK4 amplification by immunohistochemistry and/or by FISH is also a good adjunct for the diagnosis.[165]

Matthieu Bui Nguyen Binh et al in 2005 studied that "MDM2 and CDK4 Immunostainings Are Useful Adjuncts in Diagnosing Well-Differentiated and Dedifferentiated Liposarcoma Subtypes". Out of total of 559 cases of soft tissue neoplasms, immunostaining for MDM2 and CDK4 was performed on 129 cases of adipocytic tumours which undervent MDM2 and CDK4 amplification by PCR. They concluded that IHC is a convenient way to detect 12q13-15 amplification in ALT-WDLPS/DDLPS. It is highly sensitive and specific since MDM2 and/or CDK4 amplicons were rarely detected in neoplasms other than ALT-WDLPS/DDLPS. CDK4 staining is less sensitive than MDM2 staining because CDK4 is not always coamplified with the MDM220 in chromosome 12q13-15 amplicons. High specificity of staining for gene-amplified cases confirms that amplification is the main mechanism of overexpression of MDM2 and CDK4 in soft tissue tumors.[166]

Coindre studied " Grading of Soft tissue sarcomas" and concluded Histological grading is the most important factor and best indicator of metastatic risk in adult soft tissue sarcomas. The most commonly used systems are the French grading and the National Cancer Institute grading. Both are 3-grade systems and are mainly based on histologic type and subtype, tumour necrosis, and mitotic activity. The most controversial point is the respective values of histologic typing and grading. Histologic

typing should be clearly defined before any attempt at grading, and grading should not be used on tumours of intermediate malignancy such as fibroxanthoma and on some sarcomas such as dedifferentiated liposarcoma. However, grading is useful in more than 90% of adult soft tissue sarcomas.[167]

Hall et al In 2008 studied " Application of Immunohistochemistry to soft tissue neoplasm" and summarized immunohistochemistry plays an important role in the diagnosis of soft tissue tumors. One of its major utilities is to correctly identify a tumor as being of mesenchymal or non-mesenchymal origin. Once mesenchymal origin has been established, histologic subtyping according to specific cell lineage may be achieved with the use of lineage specific markers. Tumors of uncertain cell lineage and tumors with primitive small round cell morphology are often characterized by a unique immunohistochemical phenotype. In this group of tumors, immunohistochemistry is most widely applied and is of greatest value. Despite the rapid development of genetic techniques, immunohistochemistry still remains the most important diagnostic tool in the diagnosis of soft tissue tumors beside from recognition of morphological feature and clinical correlation.[168]

Vasudha bhagat et al in 2013 studied "adjunctive role of immunohistochemistry to traditional histomorphology in diagnosis and accurate typing of soft tissue sarcoma". In this study histomorphology confirmed diagnosis in 22 % cases. In 78 % cases it was contributory to IHC. IHC provide confirmative diagnosis (Single diagnosis) in 45 cases (90%), definitive diagnosis (with two possibilities) in 4 cases (8%) and noncontributory in 1 case (2%). They concluded that despite the rapid development of molecular genetic techniques, IHC still remains the most important diagnostic tool in the diagnosis of soft tissue tumors aside from recognition of morphologic features and clinical correlation. One of its major utilities is to correctly identify a tumor as mesenchymal or non-mesenchymal origin and then accurate typing done according to specific

cell lineage. IHC is specifically useful in tumors of uncertain cell lineage and primitive round cell tumors. But important not to forget histopathology which provide the basic platform for the panel approach of IHC.[169]

Jobanputra G.P.in 2016 studied histopathology of soft tissue tumors. Total 142 cases were included in the study. In this study the peak age of incidence of soft tissue tumors was between 3rd to 4th decades of age, with the male: female ratio 1.37:1. Benign tumors (89.3%) were more common than malignant tumors (10%). Most common soft tissue tumor was Lipomatous tumor.[170]

Murali et al in 2019 did the clinicopathologic study of soft tissue tumors. Out of 98 cases of soft tissue tumors, 90.8% were benign, 3.06% were intermediate and 6.12% were malignant. Male to female ratio was 1.04:1. Most common sites were extremities (64.2%) followed by head and neck (21.4%). Of all benign lesions, the commonest was lipoma (37.7%) followed by hemangioma (22.4%). Other benign tumors include fibroblastic (3.06%), fibro-histiocytic (2.04%) and pericytic tumors (1.02%). Intermediate grade soft tissue tumors include 2 cases (2.04%) of well differentiated liposarcoma and 1 case (1.02%) inflammatory myofibroblastic tumor. Malignant tumors were pleomorphic liposarcoma (1.02%), fibrosarcoma (2.04%), monophasic synovial sarcoma (1.02%) and undiffe pleomorphic sarcoma (2.04%). In this study they concluded that, Benign soft tissue tumors outnumbered malignant tumors. A thorough clinical history, gross, and light microscopic evaluation of hematoxylin and eosinstained sections are fundamental aspects in the diagnosis of soft tissue tumors.The clinicopathological evaluation is still the gold standard for the diagnosis of soft tissue neoplasms.[171]

Gayatri gogoi et al in 2017 did histomorphological study of soft tissue tumors and review of literature of rarer types. Out of 794 cases of soft tissue tumors, 733 cases were found to be benign (92.8%) and 61cases turned out to be malignant (7.2%). The most common benign tumor was leiomyoma (52%) followed by Haemangioma (16%) and Lipoma (10.1%)

and most common malignant tumor was Fibrosarcoma followed by Rhabdomyosarcoma. Among 794 cases, 183 tumors were diagnosed in male, while 611 cases were diagnosed in females. The most common site involved was extremities.[172]

Prachi hansdah et al in 2020 studied the histopathological spectrum of soft tissue tumors. A total of 226 cases were studied. Male constituted 128 cases (56.6 %) and females: 98 cases (43.4%). Age ranged from 2 months to 79 years old. Majority of lesions belonged to benign category: 192 cases (85%), malignant category: 27 cases (12%) followed by 7 cases (3%) of intermediate group. Among benign lesions, adipocytic tumours formed largest group consisting of 93 cases (41.2 %) followed by blood vessels tumors: 32 cases (14.2%) and peripheral nerve sheath and related tumors: 30 cases (13.3 %). Most common malignant lesion was fibrosarcoma: 10 cases (4.2 %). They concluded that benign tumors are more common than malignant lesions. Majority of soft tissue tumors can be diagnosed by hematoxylin and eosin stained sections which are supplemented by immunohistochemistry.[173]

Shameera Begum et al in 2020 did a study on 249 patients and in there study, the most common site of occurrence was the trunk followed by head and neck. Benign STT constituted 14.7% of all types of neoplasms. Among STT, benign tumors formed the majority (92.2%). Adipocytic tumors formed the most common histologic group. Benign STT showed a slight male preponderance with peak incidence in the fourth decade. The most common site of occurrence was the trunk followed by head and neck.[174]

MATERIAL AND METHODS

Source of Data

Present study on the immunohistochemical spectrum of mesenchymal tumors was a five year study comprising of 1.5 years prospective (1st January 2020 to 30th June 2021) and 3.5 years retrospective analysis (1st July 2016 to 31st December 2019), done in the Department of pathology, Dayanand Medical College and Hospital, Ludhiana. A total of 185 cases of mesenchymal tumors on which IHC was done were analyzed. All the cases with immunohistochemical work up were analyzed with respect to the histomorphological features favoring that of mesenchymal tumors.

METHOD OF COLLECTION OF DATA

Inclusion criteria: All mesenchymal tumors of various organs undergoing immunohistochemistry for definite categorization.

Exclusion criteria: All other neoplasms.

Duration of study:

This was five years study, conducted 1.5 years prospective starting from 1st January 2020 to 30th June 2021 and 3.5 years retrospective analysis from 1st July 2016 to 31st December 2019.

Study Design: This is prospective and retrospective study.

Methodology:

The tissue obtained in the histopathology lab were processed. Paraffin embedding and subsequent staining by Hematoxylin and Eosin was done. The slides were then subjected to histopathological examination. All 185 cases with diagnosis of mesenchymal tumors were subjected to immunohistochemical examination.

HEMATOXYLIN AND EOSIN STAINING

The paraffin embedded tissue blocks cut at 2-3 micron thickness by rotator microtome. Then the slides were kept on a hot plate in order to dewax the sections at temperature of 60 degree. Following this, the slides were deparaffinized in xylene, then hydrated through graded alcohol to water. Then it is stained with Harris hematoxylin for 15 minutes. The

sections were washed well in running tap water until sections turned blue. The sections were then differentiated in 1% acid alcohol (1% HCL in 70% alcohol) for 5-10 seconds, washed well in tap water for 5 minutes or less. These were then stained with 1% eosin for 10 minutes followed by washing in running tap water for 1-5 minutes. Sections were dehydrated once again through graded alcohol, cleared xylene and mounted with DPX avoiding air bubbles.

IMMUNOHISTOCHEMISTRY- STANDARD STREPT AVIDIN PROCEDURE

1. 2-3 um sections were cut and mounted on Poly-L-lysine coated slides. Slides were dried overnight at 37 degree C and dewaxed in xylene and hydrated.
2. Antigen retrieval procedure- The black box was filled 3/4th with citrate buffer and the slide carrier with slides was placed in it. The black box was placed in microwave for 9 mins.
3. Boiling of the solution was observed and the microwave was reset for 6min and started.
4. The box was removed and cooled under tap water.
5. Blocking endogenous peroxidase - Sections were incubated at room temperature in 0.3% H2O2 in methanol for 30-45 min and rinsed in running tap water for 5-10 mins and then dipped in distilled water for 1 min.
6. The slides were placed in Tris buffer [only one change for 5 min].
7. Blocking reagent was applied for 5-10 min and excess of it was wiped off.
8. Primary antibodies were applied covering the whole section and incubated at room temperature for 1 hour.
9. Slides were then washed in Tris buffer for 5 minutes.
10. Ultra Vision One HRP polymer covering the whole tissue was applied and incubated at room temperature for 45 mins.

11. Washing was done in TBS buffer [Tris buffer saline] for 5 min [4 changes].
12. One drop of substrate DAB [3, 3- Diaminobenzidine] solution was applied on each slide covering the whole material and incubated for 10-15 mins, then washed in deiodinized water.
13. Hematoxylin was applied for few seconds and washed under running water.
14. Dry and dehydrate in alcohol and incubate for 2 mins.
15. Mounted in DPX [distyrenedibutyl phthalate xylene]

IMMUNOHISTOCHEMISTRY- VENTANA BENCHMARK GX PROCEDURE (Automatic)

IHC staining of slides prepared from formalin fixed paraffin embedded tissue (FFPET) on the BenchMark Classic Automated system (from Ventana). Sections from FFPET biopsies are cut using the microtome at 3-4micron thickness and mounted onto SuperFrost Plus slides. For each slide, Ventana labels are then printed which include a unique barcode containing all protocol information. The slides are then loaded onto the BenchMark carousel and read by the Ventana Barcode Reader. The automated Benchmark system puts the slides through a series of user-defined de-paraffinization and antigen retrieval steps before commencing with the antibody staining. The primary antibody is either applied automatically if in a pre-diluted dispenser or otherwise manually titrated onto the slide. The pre-diluted dispensers of the ultraView Universal DAB Detection Kit then provide all reagents required for staining. The counterstain and post-counterstain comprise Hematoxylin (cat #760-2021) and bluing reagent (cat #760-2037).

OBSERVATIONS AND RESULTS

The present study was conducted in the Department of pathology, Dayanand Medical College and Hospital, Ludhiana for a period of 5 years comprising of 1.5 years prospective analysis (1st January 2020 to 30th June 2021) and 3.5 years retrospective analysis (1st July 2016 to 31st December 2019).

During the study period a total of 442 cases of mesenchymal tumors were received for histopathological examination in our department. Out of these, 185 cases of immunohistochemically confirmed mesenchymal neoplasms were analyzed with respect to light microscopic and immunohistochemical findings. The immunohistochemical panel comprised of antibodies for Vimentin, Desmin, Cytokeratin, Myogenin, SMA, S-100, CD-34, CD117, DOG-1, MDM2, h-caldesmon, EMA, Ki-67 and few other markers according to site and morphological differentials. The IHC pattern is considered diagnostic, demonstrating nuclear, membranous or cytoplasmic patterns. [Table 1]. These neoplasms were classified according to the WHO classification of tumors of soft tissue and bone 2013.

Table 1: Positivity of various markers used in study.

IHC marker	Type of positivity
Vimentin	Cytoplasmic
Desmin	Cytoplasmic
SMA	Cytoplasmic
Myogenin	Nuclear
CD34	Membranous
h-caldesmon	Cytoplasmic
S-100	Cytoplasmic/nuclear
MDM2	Nuclear/cytoplasmic
C-Kit	Membranous/cytoplasmic
Dog-1	Membranous/cytoplasmic
CD99	Membranous/cytoplasmic
CD68	Membranous/cytoplasmic
CK	Cytoplasmic
Beta-catenin	Nuclear/cytoplasmic
LCA	Membranous/cytoplasmic
Synaptophysin	Cytoplasmic
Chromogranin	Cytoplasmic
EMA	Membranous/cytoplasmic
ER	Nuclear

Age wise distribution of patients with mesenchymal neoplasms

In the present study, the age of presentation ranged from 2 to 90 years. It was observed that the mesenchymal neoplasms occurred more often between 5^{th}-7^{th} decade [99/185; 53.5% cases] and maximum cases [37/185; 20%] were seen between 51 to 60 years of life, with the mean age of 48.3 years. The youngest patient was 2 years and eldest was 90 years old.

Table 2- Age wise distribution of patients with mesenchymal neoplasms

Age range [years]	No. of patients [n= 185]	%age
1-10	07	3.88%
11-20	14	7.67%
21-30	16	8.65%
31-40	23	12.43%
41-50	32	17.30%
51-60	37	20.00%
61-70	30	16.22%
71-80	23	12.43%
81-90	03	1.62%

Sex wise distribution of patients with mesenchymal neoplasms

Slight female preponderance [97 cases, 52.43%] was observed in our study with males [88 cases, 47.67 %] being affected little less than females with the M:F ratio of 1:1.1

Table 3- Sex wise distribution of patients with mesenchymal neoplasms

Sex	No. of patients [n=185]	%age
Male	88	47.57%
Female	97	52.43%

Distribution of cases according to cell of origin [according to WHO classification for tumors of soft tissue & bone 2013]

All the tumors were classified according to cell of origin i.e. whether they belonged to adipocytic, smooth muscle, skeletal muscle, fibroblastic & myofibroblastic, peripheral nerve sheath, pericytic and vascular origins. Smooth muscle tumors formed the largest group constituting 48 cases [25.95%]. Gastrointestinal stromal tumors were the second most common comprising 36 cases[19.56%] followed by fibroblastic&myofibroblastic tumorsconstituting 27 cases[14.69 %] [Table 4]

Table 4- Distribution of cases according to cell of origin

Tumor differentiation	No. of cases [n=185]	%age
Smooth muscle tumors	48	25.95%
Gastrointestinal stromal tumors	36	19.56%
Fibroblastic & myofibroblastic tumors	28	15.14%
Tumors of Uncertain differentiation	23	12.43%
Peripheral nerve sheath tumors	18	9.73%
Skeletal muscle tumors	10	5.41%
Adipocytic tumors	9	4.96%
Pericytic tumors	5	2.70%
Fibrohistiocytic tumors	3	1.62%
Vascular tumors	2	1.18%
Endometrial stromal sarcoma	3	1.62%

Distribution of cases according to biological potential

All the cases were divided into benign, intermediate and malignant category based on the WHO classification for tumors of soft tissue & bone 2013.Of the total 185 cases included in the study, 61cases [32.97%] were benign, 100 cases [54.15%] were malignant and 24 cases [12.88%] belonged to intermediate category.

Table 5- Distribution of cases according to biological potential [based on WHO classification for tumors of soft tissue & bone 2013]

Category	No. of cases [n=185]	%age
Benign	61	32.97%
Intermediate	24	12.88%
Malignant	100	54.15%

Distribution of cases according to site.

The most common site of the mesenchymal tumors included in our study was gastrointestinal tract [n=38; 20.54%], most of the cases involving this site being GISTs. The second most common site involved was lower limb [n=26, 14.05%] followed by abdominal wall [n=22, 11.99%].

Table 6- Distribution of cases according to site.

Site	No. of cases[n=185]	%age
Gastrointestinal tract	38	20.54%
Lower limb	26	14.04%
Abdominal wall	22	11.99%
Head & neck	21	11.35%
Female genital tract	16	8.65%
Pelvis	15	8.11%
Upper limb	15	8.11%
Chest & mediastinum	15	8.11%
Retroperitoneum	13	7.03%
Back	03	1.62%
Male genital tract	01	0.54%

Individual tumors diagnosed on the basis of histopathology and IHC

Smooth muscle tumors [n=48]

Out of 185 cases, 48 cases were of smooth muscle origin. Immunohistochemical markers such as vimentin, desmin, S-100, SMA, CD-34, h-caldesmon, CD-10 and few others were used based on the site and morphological differentials.

Age wise distribution of smooth muscle tumors

In the present study, the age of presentation of smooth muscle tumors ranged from 10 to 90 years. It was observed that the maximum patients were seen between 41 to 60 years of life, with the mean age of 53 years.

Table 7- Age wise distribution of smooth muscle tumors

Age range [years]	No. of cases [n=48]	%age
1-10	-	-
11-20	1	2.18%
21-30	2	4.26%
31-40	7	14.68%
41-50	11	22.92%
51-60	14	29.26%
61-70	6	12.50%
71-80	6	12.50%
81-90	1	2.18%

Sex wise distribution of smooth muscle tumors

It was observed that females were affected [30 cases, 62.50 %] more commonly than males [18 cases,37.50%] with the M:F ratio of 1:1.6

Table 8- Sex wise distribution of smooth muscle tumors

Sex	No. of cases [n=48]	%age
male	18	37.50%
female	30	62.50%

Categories in smooth muscle tumors.

Out of the 48 cases, maximum 81.25 % cases [39/48] were of leiomyosarcoma and only 18.75 % cases [9/48] were of leiomyoma.

Table 9 – Categories in smooth muscle tumors.

Category	No. of cases [n=48]	% age
Leiomyoma [benign smooth muscle tumor]	09	18.75%
Leiomyosarcoma[malignant smooth muscle tumor]	39	81.25%

Site wise distribution of smooth muscle tumors

Maximum number of leiomyomas were seen in uterus [n=6, 66.67%] followed by one each in upper limb, abdomen and lower limb [n=1, 11.11%]. While somatic leiomyosarcoma [11/39, 28.20%] were more in number than uterine leiomyosarcomas [5/39, 12.82%]and involved lower limb followed by abdomino-pelvic area [8/11; 20.51%] and retroperitoneum [6/11; 15.48%].

Table 10- Site wise distribution of smooth muscle tumors [n= 48].

Site	Leiomyoma [n=9]	Leiomyosarcoma [n=39]
lower limb	1 [11.11%]	11 [28.20%]
upper limb	1 [11.11%]	-
head & neck	-	2 [5.13%]
retroperitoneal mass	-	6 [15.48%]
abdomino - pelvic mass	1 [11.11%]	8 [20.51%]
breast	-	2 [5.13%]
uterus	6 [66.67%]	5 [12.82%]
Gastrointestinal tract	-	3 [7.79%]
Chest wall swelling	-	1 [2.66%]
Lung	-	1 [2.66%

Leiomyoma

In the present study, there were 9 cases of leiomyoma [18.75%].

On histopathological examination, fascicular arrangement of spindle cells with indistinct cell boundaries was seen. There was minimal nuclear atypia and no significant mitosis or necrosis.

On immunohistochemistry, all the cases of leiomyomas showed 100% positivity for SMA. H-caldesmon being a newer marker in the department was applied only on 2 cases which showed strong immunopositivity for this marker. Both of these cases were SMA positive too. Desmin positivity was seen in 6 out of 8 cases[75%]. In 2 cases of uterine leiomyomas ER was applied which showed positivity in one case [50%]. One case of uterine leiomyoma showed weak positivity for CD10. So all leiomyomas were found to be positive for vimentin and SMA [100% positivity], while desmin was positive in 75% of the cases. Ki67 was found to be in the range of 1-3%.

Leiomyosarcoma

There were a total of 39 cases [81.25%] of leiomyosarcoma.On histopathology examination, fascicular arrangement of spindle cells with moderate to marked nuclear atypia and significant mitosis & necrosis were the findings. All the cases of uterine leiomyosarcoma showed coagulative type of necrosis with a mitotic count of >10/10hpf. While the leiomyosarcomas of somatic soft tissue origin showed variable mitotic activity.

On immunohistochemistry, SMA was positive in 37/38 cases while one case was SMA negative but it showed positivity for h-caldesmon. Desmin was applied in 34 cases and its positivity was seen in 20/34 cases [58.82%]. In 8 cases ER was applied which came out to be positive in 3 cases of LMS of uterine origin. One of the case showed CD10 positivity which had an epithelioid morphology on H&E. Ki67 ranged from 5 to 90%. So it was observed that leiomyosarcomas were consistently positive for

vimentin, h-caldesmon and SMA; while Desmin positivity was found in 58.82% cases only.

Table 11- Immunohistochemistry findings in smooth muscle tumors.

IHC marker	Leiomyoma [n=9]	Leiomyosarcoma [n=39]
Vimentin	6/6	31/31
Desmin	6/8	20/34
h-Caldesmon	2/2	10/10
SMA	8/8	37/38
S-100	0/5	2/34
Cytokeratin	-	2/15
Myogenin	0/1	0/14
CD-34	0/4	4/31
CD-10	1/1	1/6
ER	1/2	3/8
C-kit	0/3	0/12
Ki-67	1-3 %	5-90 %

Gastrointestinal stromal tumors [n=36]

Age wise distribution of gastrointestinal stromal tumors

In the present study, the age of presentation of gastrointestinal tumors ranged from 21 to 80 years. The cases were equally distributed in 5^{th} to 8^{th} decade with the mean age of 58.4 years and only 4/36 cases seen before 40 years.

Table 12- Age wise distribution of gastrointestinal stromal tumors

Age range [years]	No. of cases [n=36]	%age
21-30	1	2.88%
31-40	3	8.33%
41-50	9	25.00%
51-60	7	19.44%
61-70	8	22.22 %
71-80	8	22.22%

Sex wise distribution of gastrointestinal stromal tumors

Males were affected [22 cases, 61.11%] more commonly than females [14 cases, 38.89%] with the M:F ratio of 1.6:1

Table 13- Sex wise distribution of gastrointestinal stromal tumors

Sex	No.of cases [n=36]	%age
Male	22	61.11%
Female	14	38.89%

Distribution of gastrointestinal stromal tumors according to biological potential

These tumors were divided into benign and malignant categories based on the prognostic group according to the WHO classification for tumors of soft tissue & bone 2013 that considers size and mitotic count per 50 hpf. Prognostic groups 1, 2 and 3a were categorized as benign, and the prognostic groups 3b, 5, 6a and 6b were categorized as malignant. There was no case in the study that belonged to intermediate category i.e. the prognostic group 4.

Table 14: Distribution of gastrointestinal stromal tumors according to biological potential

Category	No. of cases [n=36]	%age
Benign [prognostic group 1,2,3a]	29	80.55%
Malignant[prognostic group 3b,5,6a,6b]	7	19.45%

Site wise distribution of Gastrointestinal stromal tumors

Stomach was the commonest site [n= 20, 51.72%] followed by small intestine [n=14, 38.89%] and large intestine [n=2, 5.56%].

Table 15-Site wise distribution of Gastrointestinal stromal tumors

Site	Benign GIST [n=29]	Malignant GIST [n=7]	Total [n=36]
Stomach	15 [51.72%]	5 [71.43%]	20 [55.55%]
Small intestine	12 [41.37%]	2 [28.67%]	14 [38.89%]
Large intestine	2 [6.99%]	0 [0%]	2 [5.56%]

Gastrointestinal stromal tumors [benign – prognostic group 1, 2, 3a]

On histological examination most of the tumors showed spindle cell morphology seen as sheets and fascicles of spindle cells having ill-defined cytoplasmic boundaries. Eighteen cases showed prominent paranuclear vacuoles. Two of the cases had epithelioid cell morphology. Mitotic count was < 5/50 hpf in all the cases. No significant nuclear atypia/necrosis was seen in any case. They were further classified in three of the prognostic groups [1, 2 and 3a] based on the tumor size.

IHC was done in 28/29 cases, out of which 25 [92.69%] were positive for CD 117. DOG1 was applied in 23 cases and all were diffusely positive[100%].Two cases which were negative for CD117 showed strong positivity for DOG1 that led to the final diagnosis of GIST. CD 34 was positive in 18 out of 23 cases [78.36%]. It was observed that DOG1 was consistently positive in all the cases of GIST.

Gastrointestinal stromal tumors [malignant – prognostic group 3b, 5, 6a, 6b]

On histological examination these tumors showed sheets of pleomorphic cells having oval to spindle shaped nuclei and ill-defined cytoplasmic boundaries. Three cases showed prominent paranuclear vacuoles. Areas of necrosis were noted along with a mitotic count of > 5/50 hpf in all the cases. Two cases showed atypical mitotic figures. These cases were further classified in four of the prognostic groups in this category [3b, 5, 6a and 6b] based on the tumor size.

On immunohistochemical examination, DOG1, CD117 and CD34 were applied in 7, 6 and 5 cases respectively with 100% positivity in all.

Immunohistochemistry findings of Gastrointestinal stromal tumors

Table 16- Immunohistochemistry findings of Gastrointestinal stromal tumors

IHC marker	Benign GIST [n=29]	Malignant GIST [n=7]
Vimentin	12/12	5/5
Desmin	1/15	0/4
SMA	15/28	2/6
S-100	2/28	1/7
CD34	18/23	5/5
Cytokeratin	0/2	-
C-kit	25/27	6/6
DOG 1	23/23	7/7
Ki-67	1-25%	5-30%

Important here to note that in the present study although CD 34 was negative in few cases of benign GIST, it was found positive in all cases of malignant GIST. SMA i.e. smooth muscle differentiation was seen in approximately 50% of cases of benign GIST. DOG-1 and C-kit were consistently found to be expressed in benign and malignant GIST.

Fibroblastic & myofibroblastic tumors [n=28]

These tumors were third most common tumors in our study.

Age wise distribution of fibroblastic & myofibroblastic tumors

This category of tumors constituted a total of 28 cases. The cases showed a wide range of age distribution with a mean age of 47 years. Maximum number of cases fell in the age group 51-70 years [n=12, 42.86%] followed by age group 21-40 years [n=8, 28.67%]

Table 17- Age wise distribution in fibroblastic & myofibroblastic tumors.

Age distribution	No.of cases [n=28]	%age
10–20	2	7.14%
21-30	4	14.38%
31-40	4	14.38%
41-50	2	7.14%
51-60	6	21.43%
61-70	6	21.43%
71-80	3	10.71%

Sex wise distribution of fibroblastic & myofibroblastic tumors

It was observed that males were affected more commonly [16 cases, 57.14 %] than females [12 cases, 42.86 %] with the M:F ratio of 1.3:1

Table 18- Sex wise distribution of fibroblastic & myofibroblastic tumors.

Sex	No.of cases [n=28]	%age
Male	16	57.14%
Female	12	42.86%

Category wise distribution of fibroblastic & myofibroblastic tumors [WHO classification for tumors of soft tissue & bone 2013]

Out of the total 28 cases of fibroblastic & myo-fibroblastic origin, maximum number ie 24 cases [85.71%] belonged to intermediate category, 3 cases [10.71%] were benign and 1 case [3.67%] was malignant

Table 19 – Category wise distribution of fibroblastic & myo-fibroblastic tumors

Diagnosis [n=28]	Benign	Intermediate	Malignant
Angiofibroma	1	-	-
Fibroma	1	-	-
Nodular fasciitis	1	-	-
DFSP	-	6	-
Fibromatosis	-	7	-
Myofibroblastic sarcoma	-	1	-
Solitary fibrous tumor	-	7	-
Inflammatory myofibroblastic tumor	-	3	-
Fibromyxoid sarcoma	-	-	1
Total	3 [10.71%]	24[85.71%]	1 [3.67%]

Distribution of fibroblastic & myofibroblastic tumors according to site

The most common site involved by this category of tumors was abdominal wall [n= 8, 28.67%] followed by chest and mediastinum [n=7, 25.00%] and upper limb [n=5, 17.95%]

Table 20 – Distribution of fibroblastic & myofibroblastic tumors according to site.

Diagnosis [n=28]	Abdominal wall	Upper limb	Pelvis	Chest & mediastinum	Back	Head & neck	Lower limb
Angiofibroma	-	1	-	-	-	-	-
Fibroma	-	1	-	-	-	-	-
Nodular fasciitis	-	-	-	-	1	-	-
DFSP	2	1	3			-	-
Fibromatosis	2	1	1	1	1	-	1
Myofibroblastic sarcoma	1	-	-	-	-	-	-
Solitary fibrous tumor	2	1	-	4	-	-	-
Inflammatory myofibroblastic tumor	1	-	-	1	-	1	-
Fibromyxoid sarcoma	-	-	-	1	-	-	-
Total [n=28]	8 [28.57%]	5 [17.86%]	4 [14.38%]	7 [25.00%]	2[7.14%]	1 [3.67%]	1 [3.67%]

In present study though fibromatosis presented with a widespread distribution, DFSP had predilection for abdominal wall and pelvis. SFT involved more commonly abdominal wall, chest and abdomen.

On microscopic examination,all the benign tumors in this category were composed of spindle shaped plump fibroblasts lacking nuclear hyperchromasia and pleomorphism. Angiofibroma additionally showed interspersed small to medium sized thick walled and irregularly branching vessels. Nodular fasciitis showed myxoid hypocellular areas with presence of collagen bundles.

In the intermediate category the cells were either bland like in cases of fibromatosis or showed mild to moderate nuclear pleomorphism and hyperchromasia which were typically seen in DFSP along with a characteristic storiform pattern. Hemagiopericytoma like vascular pattern was noted in all SFT cases. Inflammatory myofibroblastic tumors showed myofibroblastic spindle cell proliferation mixed with inflammatory cells. In the case of myofibroblastic sarcoma sheets of spindle cells having elongated to wavy nuclei and ill-defined eosinophilic cytoplasm was seen. These cells were present in a collagenous matrix with prominent hyalinization. Similar morphology was seen in case of fibromyxoid sarcoma with abrupt myxoid transition and focal areas showing increased mitosis and areas of necrosis.

IHC: various markers like vimentin, smooth muscle markers, CD34, CD68, beta catenin etc were used as shown in table 20, for confirmation or categorization. All cases of fibromatosis showed nuclear positivity for beta catenin. In DFSP 100% and 33.33% cases were positive for CD34 and SMA respectively. All SFTs stained for CD34 and Bcl2. Fibromyxoid sarcoma showed the positivity for vimentin, SMA and EMA. Thus all these markers helped in confirming the final diagnosis.

Table 21- immunohistochemistry findings of fibroblastic & myofibroblastic tumors.

Diagnosis [n=28]	Vimentin	Desmin	SMA	S-100	Myogenin	CK	EMA	CD-34	CD-68	CD-20	Beta catenin	p53	bcl2	cd99	Alk1
Angiofibroma [n=1]	1/1	-	1/1	-	-	-	-	1/1	-	-	-	-	-	-	-
Fibroma[n=1]	1/1	-	1/1	0/1	-	-	-	0/1	-	-	0/1	-	-	-	-
Nodular fasciitis[n=1]	1/1	0/1	1/1	0/1	-	-	-	0/1	-	-	-	-	-	-	-
DFSP [n=6]	4/4	1/4	2/6	0/6	0/2	0/1	-	6/6	0/2	-	0/2	2/2	-	-	-
Fibromatosis [n=7]	4/4	1/7	6/7	1/6	1/3	-	-	0/7	-	-	7/7	-	-	-	-
Myofibroblastic sarcoma [n=1]	1/1	0/1	1/1	0/1	0/1	-	-	0/1	-	-	0/1	-	-	-	-
Solitary fibrous tumor [n=7]	7/7	2/5	1/7	0/7	0/1	0/4	-	7/7	-	-	-	-	3/3	3/3	-
Inflammatory myofibroblastic tumor [n=3]	-	0/1	1/2	0/2	0/1	0/1	0/1	0/3	1/1	1/1	-	-	-	-	1/2
Fibromyxoid sarcoma [n=1]	1/1	0/1	1/1	0/1	0/1	-	1/1	0/1	-	-	0/1	-	-	-	-

Peripheral nerve sheath tumours [n=18]

This category comprised of a total of 18 cases [9.73%] [n=185]. Out of the 18 cases, majority were benign [13 cases, 72.22%] and 5 cases were of malignant peripheral nerve sheath tumor. Benign category included neurofibroma [n=2] and schwannoma [n=11].

Age wise distribution of peripheral nerve sheath tumors

Maximum number of cases fell in the age group of 31-40 years, with a mean age of 42.8 years.

Table 22- Age wise distribution of peripheral nerve sheath tumors

Age group	No. of cases[n=18]	%age
10-20	3	16.76%
21-30	1	5.55%
31-40	6	33.33%
41-50	1	5.55%
51-60	2	11.11%
61-70	3	16.76%
71-80	2	11.11%

Sex wise distribution of peripheral nerve sheath tumors

Of the 18 cases of peripheral nerve sheath tumors 14 [77.78%] were females and 4 [22.22%] were males with a male to female ratio being 1:3.5

Table 23: Sex wise distribution of peripheral nerve sheath tumors

Sex	No. of cases[n=18]	%age
Male	4	22.22%
Female	14	77.78%

Category wise distribution of peripheral nerve sheath tumors

Out of the 18 cases, majority were benign [13 cases, 72.22%] and 5 cases were malignant. Benign category included neurofibroma [n=2] and schwannoma [n=11].

Table 24: Category wise distribution of peripheral nerve sheath tumors

Category	No. of cases[n=18]	%age
Benign - schwannoma	11	61.11%
Benign - neurofibroma	2	11.11%
Malignant-malignant peripheral nerve sheath tumour	5	27.78%

Distribution of cases according to site

Majority of cases were seen in lower limb [n=6, 33.33%] followed by upper limb [n=3, 16.67%] and GIT [n=3, 16.67%. Neurofibromas were seen in lower limb and paraspinal location, while schwannoma had a ubiquitous distribution and involved mainly extremities and GIT along with lung, retroperitoneum and paraspinal region while MPNST were seen mainly in extremities.

Table 25- Distribution of cases according to site

Site	Neurofibroma [n=2]	Schwannoma [n=11]	MPNST [n=5]	Total [n=18]
Lower limb	1	2	3	6 [33.33%]
Upper limb		2	1	3 [16.67%
Git	-	3	-	3 [16.67%]
Paraspinal mass	1	1	-	2 [11.11%]
Head & neck	-	-	1	1 [5.55%]
Lung	-	1	-	1 [5.55%]
Retroperitoneum	-	1	-	1 [5.55%]
Illiac fossa	-	1	-	1 [5.55%]

On histology, alternating Antony A and Antony B areas were seen in cases of schwannoma with no significant atypia, mitosis and necrosis. Nuclear palisading around fibrillary process ie. Verocay bodies were seen in 4 cases. The neurofibromas were composed of bland spindle cells separated by collagen fibers and myxoid material. No mitotic activity was seen. MPNST was composed of spindle shaped cells arranged in sheets, whorls and fascicles with individual cells exhibiting significant nuclear pleomorphism, mitosis and areas of geographic necrosis.

On IHC, all the cases of peripheral nerve sheath tumors showed 100% positivity for S-100. Additionally one of the case of MPNST and one case of schwannoma showed focal positivity for SMA. Weak and focal positivity for desmin and SMA was seen in 2 cases and 1 case of schwannoma respectively.

Table 26- Immunohistochemistry findings of peripheral nerve sheath tumors

IHC marker	Neurofibroma [n=2]	Schwannoma [n=11]	MPNST [n=5]
Vimentin	1/1	6/6	4/4
Desmin	-	2/7	0/4
SMA	0/2	1/11	1/5
Myogenin	-	0/1	0/2
S-100	2/2	11/11	5/5
EMA	0/1	-	-
CD34	-	0/8	1/5
c-kit	-	0/5	0/1
ki67	1-3%	1-10%	25-60%

Thus S-100 helped in clinching the diagnosis in all the cases of nerve sheath tumors and mitosis and necrosis helped to differentiate benign from malignant.

Skeletal muscle tumors [n=10]

All the 10 skeletal muscle tumors included in the study were malignant, out of which 3 cases were of embryonal rhabdomyosarcoma, 1 case of alveolar rhabdomyosarcoma, 1 case of spindle cell rhabdomyosarcoma, 1 case of pleomorphic rhabdomyosarcoma and 4 cases were of rhabdomyosarcoma which were further not classified.

Table 27- Classification of Rhabdomyosarcomas

Diagnosis	No. of cases [n=10]	%age
Embryonal RMS	3	30.00%
Rhabdomyosarcoma nos	4	40.00%
Alveolar RMS	1	10.00%
Pleomorphic RMS	1	10.00%
Spindle cell RMS	1	10.00%

Age distribution of skeletal muscle tumors

Maximum number of cases were seen between 1 to 10 years of age [n=5, 50.00%] with the youngest age being 2 years and the eldest being 75 years. But majority of the cases were seen in first two decades of life.

Table 28- Age distribution of skeletal muscle tumors

Age group	No. of cases [n=10]	%age
1-10	5	50.00%
11-20	2	20.00%
21-30	-	-
31-40	-	-
41-50	-	-
51-60	1	10.00%
61-70	1	10.00%
71-80	1	10.00%

Sex distribution of skeletal muscle tumors

Of the 10 cases of skeletal muscle tumors, 04 [40%] were female and 06 cases [60%] were male with a male to female ratio being 1.5:1

Table 29- Sex distribution of skeletal muscle tumors

Sex	No. of cases[n=10]	%age
Male	06	60.00%
Female	04	40.00%

Site wise distribution of skeletal muscle tumors

Most common sites involved by skeletal muscle tumors were abdomen and head & neck with 3 cases each [30%] followed by retroperitoneum [n=2, 20%]

Table 30 – Site wise distribution of skeletal muscle tumors

Site	No. of cases [n=10]	%age
Abdomen	3	30.00%
Head & neck	3	30.00%
Retroperitoneum	2	20.00%
Pleura	1	10.00%
Pelvis	1	10.00%

On histology, all cases of ERMS showed alternating hypocellular and hypercellular areas with myxoid change. Individual tumor cells were primitive appearing, with round, stellate, to spindle cell morphology and hyperchromatic nuclei. More well-differentiated cells with abundant eosinophilic cytoplasm, called rhabdomyoblasts, were seen in one of the case. ARMS was composed of sheets and nests separated by fibrovascular septae (alveolar pattern). These nest were composed of primitive round tumor cells with hyperchromatic nuclei and scant cytoplasm. Few multinucleated cells with rhabdomyoblastic differentiation

were also seen. Pleomorphic RMS showed sheets of large, atypical and few multinucleated spindle to polygonal cells with bizzare nuclei and eosinophilic cytoplasm. The case of spindle cell RMS showed presence of spindle cells in lobules and sheets separated by hyalinized stroma. Frequent mitotic figures were seen.

On immunohistochemistry, all these tumors were immunopositive for vimentin, desmin and myogenin. Other markers for the differential of tumors with round cell morphology i.e. LCA, CD99, synaptophysin and chromogranin came out to be negative.

Table 31 – Immunohistochemistry findings of skeletal muscle tumors

IHC marker	Embryonal RMS [n=3]	Alveolar RMS [n=1]	Spindle cell RMS [n=1]	Pleomorphic RMS [n=1]	RMS nos [n=4]
Vimentin	2/2	1/1	1/1	1/1	3/3
Desmin	3/3	1/1	1/1	1/1	3/3
SMA	0/1	0/1	0/1	0/1	1/2
Myogenin	3/3	1/1	1/1	1/1	4/4
S-100	0/2	0/1	0/1	0/1	1/2
CK	0/1	0/1	0/1	1/1	0/2
LCA	0/1	0/1	-	-	0/2
CD99	0/2	0/1	-	0/1	0/2
Synaptophysin	0/1	-	-	-	0/2
Chromogranin	0/1	-	-	-	0/1
Ki67	50-60%	98%	-	90%	50-60%

Adipocytic tumors [n=9]

Maximum cases of adipocytic tumors belonged to malignant category [n=8, 88.89%]. Only one case was of benign category diagnosed as spindle cell lipoma [n=1, 11.11%]

Table 32- category wise distribution of adipocytic tumors

Diagnosis		no. of cases [n=9]
Benign- spindle cell lipoma		1 [11.11%]
Malignant	Myxoid LPS	5 [55.56%]
	Well differentiated LPS	2 [22.22%]
	Dedifferentiated LPS	1 [11.11%]

Table 33- Age wise distribution of adipocytic tumors

Age group	Benign [n=1]	Malignant [n=8]	Total [n=9]
31-40	-	1	1 [11.11%]
41-50	-	3	3 [33.33%]
51-60	-	-	-
61-70	1	3	4 [44.44%]
71-80	-	1	1 [11.11%]

Maximum number of cases were seen in age group of 41-50 and 61-70 years with a mean age of 54.4 years.

Sex wise distribution of adipocytic tumors

Of the 9 cases of Adipocytic tumors, 2 [22.22%] were female and 7 cases [77.78%] were male with a male to female ratio of 3.5:1

Table 34- Sex distribution of Adipocytic tumors

Sex	Benign [n=1]	Malignant [n=8]	Total [n=9]
Male	1	6	7 [77.78%]
Female	-	2	2 [22.22%]

Site wise distribution of adipocytic tumors

The most common site in cases of adipocytic tumors was lower limb [n=3, 33.33%] followed by retroperitoneum [n= 2 , 22.22%].

Table 35- Site wise distribution of Adipocytic tumors

Site	Benign [n=1]	Malignant [n=8]
Lower limb	-	3
Inguinal mass	1	-
Retroperitoneum	-	2
Chest	-	1
Neck	-	1
Back	-	1

On histology, the benign spindle cell lipoma showed arrangement of bland spindle cells in sheets and short fascicles, interspersed were seen mature adipocytes and ropy collagen. No lipoblast/ mitosis/ necrosis were seen in this case.

All the cases of liposarcoma showed variable sized adipocytes with interspersed lipoblasts. Minimal atypia was noted in well differentiated LPS. Prominent myxoid areas with chicken wire vasculature were seen in case of myxoid LPS .Pleomorphic and bizzare and multinucleated cells

were seen in case of pleomorphic LPS. Dedifferentiated LPS showed abrupt transition from well differentiated areas to poorly differentiated areas with no lipogenic differentiation. Variable areas of necrosis and mitosis were seen in cases of LPS.

On immunohistochemistry, MDM2 was applied in 5 cases and it was positive in all the 5 cases of LPS [5/5, 100%], S-100 was applied in 7 cases and it was positive in 6 cases [6/7, 85.17%]. One case of dedifferentiated LPS showed desmin positivity. CD34 was strongly positive in case of spindle cell lipoma while this case was S100 negative.

Table 36- Immunohistochemistry findings in Adipocytic tumors

IHC marker	Benign [n=1]	Malignant [n=8]
Vimentin	1/1	5/5
Desmin	1/1	1/4
Myogenin	-	0/2
CK	-	0/1
SMA	0/1	2/5
S-100	0/1	6/7
MDM2	-	5/5
CD34	1/1	2/8
Bcl2	0/1	0/2
ki67	1%	2-50%

Tumors of uncertain differentiation [n=23]

Age wise distribution of cases

This category of tumors constituted a total of 23 cases. The age of presentation ranged from 10 to 80 years. It was observed that the maximum cases were seen between 11 to 30 years of life [n=11, 47.83%], with the mean age of 34.8 years.

Table 37- Age wise distribution of cases

Age range [years]	No. of cases[n=23]	%age
1-10	2	8.79%
11-20	6	26.09%
21-30	5	21.74%
31-40	1	4.35%
41-50	2	8.79%
51-60	4	17.49%
61-70	1	4.35%
71-80	2	8.79%

Sex wise distribution of tumors of Uncertain differentiation

Females were affected more commonly [14 cases, 60.87 %] than males [9 cases, 39.13 %] with the M:F ratio of 1:1.5

Table 38- Sex wise distribution of tumors of Uncertain differentiation

Sex	No. of cases[n=23]	%age
Female	14	60.87
Male	9	39.13

Category wise distribution of cases with uncertain differentiation

This group included 3 tumor categories i.e.ES/PNET [n=8, 34.88%], synovial sarcoma [n=13, 56.52%] and pleomorphic sarcoma [n=2,8.79%].

Table 39- Category wise distribution of cases with uncertain differentiation

Diagnosis	No. of cases[n=23]	%age
Synovial sarcoma	13	56.52%
Ewing's sarcoma	8	34.88%
Pleomorphic sarcoma	2	8.79%

Distribution of cases according to site

Maximum number of cases were seen in the lower extremity [n=10, 76.92%] and these all were synovial sarcoma. Head and neck was the second most common site in which 6 cases of ES/PNET and 1 case of pleomorphic sarcoma were seen.

Table 40- Distribution of cases according to site [n=23]

Site	Synovial sarcoma[n=13]	Ewing's sarcoma[n=8]	Pleomorphic sarcoma[n=2]
Lower limb	10	-	-
Head & neck	-	6	1
Pleura	1	-	-
Lung	-	1	-
Shoulder mass	1	-	-
Abdominal mass	1	1	1

Synovial sarcoma [n=13]

On histology, out of total 13 cases of synovial sarcoma, 5 cases showed a monophasic pattern with predominant spindle cell component seen as sheets and fascicles of cells with oval to spindle shaped hyperchromatic nuclei. In the remaining 8 cases biphasic pattern was seen with epithelial

component seen as cords and focal glandular configuration of cuboidal to columnar cells with pleomorphic vesicular nuclei and moderate amount of cytoplasm. Marked nuclear atypia, mitosis and necrosis were seen in all the cases.

On immunohistochemistry, vimentin was applied in 8 cases and was positive in all. Out of the 8 cases with biphasic pattern on morphology, cytokeratin was positive in 7 cases. One cytokeratin negative case showed positivity for EMA. Bcl2 was positive in 100% cases tested [12/12]. Beta catenin was positive in all the 5 cases tested. [100%]

Ewing's sarcoma/PNET [n=8]

On histological examination sheets and of small round blue cells having a high N/C ratio and scant amount of cytoplasm were seen.

On immunohistochemistry, 100% membranous positivity for CD99 was observed in all the cases [8/8]. The morphological differentials were ruled out on the basis of CD99 positivity and negativity for markers like LCA, synaptophysin, chromogranin A, cytokeratin and desmin.

Pleomorphic sarcoma [n=2]

On histology, both these cases showed sheets of pleomorphic cells with frequent bizzare multinucleated tumor giant cells. Atypical mitotic figures and areas of necrosis were also noted.

On immunohistochemistry, both the cases were vimentin positive [2/2] and cytokeratin negative [0/2]. One of the case showed weak positivity for SMA and the other showed weak and focal positivity for desmin.

Immunohistochemistry findings of tumors with uncertain differentiation

Table 41- Immunohistochemistry findings of tumors with uncertain differentiation

IHC marker	Synovial sarcoma [n=13]	Ewing's sarcoma/PNET[n=8]	Pleomorphic sarcoma[n=2]
Vimentin	8/8	6/6	2/2
Desmin	1/10	1/5	1 /2
Cytokeratin	7/9	0/5	0/2
Myogenin	0/6	1/5	0/2
SMA	2/12	0/1	1 /2
S-100	3/11	-	1 /2
CD34	0/10	0/1	0/2
Bcl2	12/12	-	-
CD99	3/3	8/8	-
EMA	4/7	1/2	0/1
Beta catenin	5/5	-	-
LCA	-	1/8	-
C-kit	0/1	-	0/1
Dog1	-	-	0/1
Synaptophysin	-	0/5	-
Chromogranin A	-	2/6	-
Ki67	1-70%	40-90%	50%

Tumors of pericytic differentiation [n=5]

Out of 4 pericytic tumors, 2 cases were reported as glomus tumor, 2 cases as angioleiomyoma and one case as myopericytoma.

Age wise distribution of pericytic tumors

Pericytic tumors showed no age predilection.

Table 42- age distribution of pericytic tumors

Age	no. of cases [n=5]
21-40	1
41-60	2
61-70	2

Sex wise distribution of pericytic tumors

Of the 5 pericytic tumors diagnosed, 3 cases were seen in males and 2 cases both glomus tumors were seen in females with a M:F being 1.5:1

Distribution of pericytic tumors according to site

Both the cases of glomus tumor and one case of myopericytoma were seen in upper limb. One case of angioleiomyoma was seen in lower limb and one presented as nasal mass.

Table 43- Distribution of pericytic tumors according to site

Site	Glomus tumor[n=2]	Angioleiomyoma[n=2]	Myopericytoma[n=1]
Upper limb	2	-	1
Lower limb	-	1	-
Nasal mass	-	1	-

Glomus tumor

On histology, the diagnosis was made on the basis of presence of nests of glomus cells having small centrally placed, uniform round nuclei and moderate amount of eosinophilic cytoplasm with well-defined cell borders. These nests were seen surrounding the capillary sized vessels.
On immunohistochemistry, both the cases were SMA and CD34 positive and CK negative with Ki67 of less than 1% in both the cases.

Angioleiomyoma

On histological examination, both the cases showed fascicles of smooth muscle cells with interspersed slit-like vascular channels.
On immunohistochemistry, both the cases were SMA and CD34 positive, one of the case showed desmin positivity.Ki67 index was 1% and 2% respectively.

Myopericytoma

On histological examination,it showed presence of plump spindled cells with eosinophilic cytoplasm arranged concentrically around the branching blood vessels.
On immunohistochemistry, it showed diffuse strong positivity for SMA and h-caldesmon with focal desmin positivity. CD34 was negative in tumor cells and highlighted the blood vessels.

Vascular tumors [n=2]

Both tumors in this category were malignant and one was diagnosed as epithelioid hemangioendothelioma and one as angiosarcoma.

Age distribution of vascular tumors

Both the cases occurred in 8^{th} decade of life.

Sex wise distribution of vascular tumors

Both the cases were seen in males

Site wise distribution of vascular tumors

Case of angiosarcoma was seen as inguinal region mass while epithelioid hemangioendothelioma was diagnosed as a mass lesion from the tip of nose.

On histological examination both the cases showed epithelioid cell morphology with pleomorphic vesicular nuclei and moderate amount of eosinophilic cytoplasm. Myxohyaline stroma was prominent in case of epithelioid hemangioendothelioma while significant atypia and necrosis were seen in case of angiosarcoma

On immunohistochemistry, both the cases were vimentin positive and cytokeratin negative. They were positive for CD34. S-100 and SMA was negative in both.

Endometrial stromal sarcoma [n=3]

Out of 3 cases, 2 cases were of low grade ESS which presented as uterine masses and 1 case was of high grade ESS that presented as pelvic mass. They were seen in females aged 41-60 years.

On histology, they showed round to spindle cell morphology with pleomorphic hyperchromatic nuclei arranged in fascicles and sheets. The case of high grade ESS showed a high mitotic count (>10/10hpf) along with significant nuclear atypia and areas of necrosis.

On immunohistochemistry, both cases of low grade ESS were strongly immunoreactive for CD10. They showed ER positivity but were negative for SMA, Desmin and CD34. The Ki67 labelling index was 1% and 5% respectively. One case of high grade ESS showed positivity for cyclin D1. It also showed focal positivity for CD10 with a ki67 of 95%.

DISCUSSION

The optimal treatment of mesenchymal tumors depends on establishing an accurate tissue diagnosis. Classically, histopathology has been the cornerstone to tumor diagnosis. However, immunohistochemistry (IHC) is an extraordinarily powerful tool in diagnostic surgical pathology. It is an efficient and cost-effective approach to identify various mesenchymal tumors and reach towards a specific histogenic origin of tumors. It has made possible to diagnose and subtype malignant soft tissue tumors accurately. The lineage specific markers have proven to be particularly sensitive and specific markers, even in many cases of histologically poorly differentiated malignancies. Incidence rates, gender and location of lesions all strongly influence the overall positive predictive value of antibodies.

Present study was a five year study comprising of 1.5 years prospective(1st January 2020 to 30th June 2021) and 3.5 years retrospective analysis (1st July 2016 to 31st December 2019), done in the Department of pathology, Dayanand Medical College and Hospital, Ludhiana . During the study period a total of 442 cases of mesenchymal tumors were received for histopathological examination in our department. Out of these, 185 cases of immunohistochemically confirmed mesenchymal neoplasms were analyzed with respect to light microscopic and immunohistochemical findings.

The age of patients in our study ranged from 2 years to 90 years, with a mean age of 48.3 years. This was comparable with study conducted by *Vasudha bhagat et al.*[169] In their study the age ranged from 3 to 80 years with a mean age of 40 years.

In our study 88 males and 97 females were included. The male to female ratio was 1:1.1. Over all incidence of mesenchymal tumors was slightly higher in females. This observation is in concordance with the study conducted by *Wibmer et al* [175] and *Agravat et al* [15] as shown in table below.

Table 44- Comparison of sex distribution of mesenchymal tumors in various studies.

Study	Males	Females	M:F
Present study [n=185]	88	97	1:1.1
Agravat et al [n=100]	41	59	1:1.4
Vasudha et al [n=50]	24	26	1:1.08

However, *Ducimetiere et al* [176] and *Jemal et al* [177] found a slight male preponderance with a M:F of 1.3:1 and 1.2:1 respectively.

Smooth muscle tumors

These tumors were diagnosed on H&E by presence long interlacing fascicles of spindle shaped cells having moderate amount of eosinophilic cytoplasm with indistinct cell boundaries. LMS additionally showed marked nuclear atypia with brisk mitosis and necrosis. Similar histopathology finding was observed by *Katherine M et al.*[178] IHC is needed to confirm the diagnosis of smooth muscle tumors besides characteristic histopathology.

Leiomyosarcomas outnumbered leiomyomas in this study, total cases being 39 and 9 respectively. Out of the 9 cases of leiomyomas, 6 were uterine in origin followed by one each in upper limb, abdomen and lower limb. While the most common site affected by LMS was lower limb (n=11) followed by pelvis (n=8) and retroperitoneum (n=6). *Shah et al* [179] and *Singh et al* [180] also found lower limb to be the most common site for LMS.

SMA & h-Caldesmon were the most sensitive markers in our study both showing 100% positivity in case of leiomyoma and 97.4% & 100% positivity respectively, in case of LMS. Desmin showed 75% and 58.8% positivity in case of leiomyoma and LMS respectively. These observations

were comparable to the studiesconducted by *Carvalho et al* [181], *E. olivia et al* [182] and *shah et al* [179] as shown in the table 45

Table 45: Comparison of sensitivity of markers for smooth muscle tumors

Study	Leiomyoma			LMS		
	h-caldesmon	SMA	Desmin	h-caldesmon	SMA	Desmin
Present study	100%	100%	75%	100%	97.4%	58.8%
Carvalho et al	-	-	-	66 %	95%	73%
E. olivia et al	100%	-	100%	77.8%	-	88.9%
Shah et al	-	-	-		97%	56.7%

Gastrointestinal stromal tumors

In this study, we identified 36 patients with GISTs. The mean age of the patients was 58.4 years which was supported by the observations of *Antonescu et al.* [183], *Alqusous et al.* [184], *Din et al.* [185], and *Kkrishnappa et al.*[186] Males (61.11%) were found to be affected more commonly as compared to females (38.89%) as in the studies of *Antonescu et al.*[183], *Alqusous et al.*[184] and *Din et al.*[185] The most common location was the stomach in 20 patients (51.72%), followed by the small intestine. This observation is in agreement with that of *Ahmed et al.*[187], *Klieser et al*.[188], *Lopes et al*.[189] *Alqusous et al*.[184], *Din et al.*[185] and *Kkrishnappa et al*.[186] where stomach found to be the most common site for GIST.

Immunohistochemically, CD117 was positive in 93.94 % cases (including both benign and malignant ones). Two cases of benign GIST were CD117 negative, but were positive for DOG1. DOG1 positivity was seen in 100% cases of both benign and malignant category, so this marker came out to be more sensitive marker for GIST. Table 46 compares the expression of different markers used in our study with the studies done by *kkrishnappa et al* [186], *Mcdonnell mj et al* [190] and *jumniensuk et al*.[191]

Table 46: comparison of IHC expression of GIST

IHC markers	Present study	Kkrishnappa et al	Mcdonnell mj et al	Jumniensuk et al
DOG1	100%	-	-	91.7%
CD117	93.94%	78.6%	90.6%	98.7%
CD34	82.14%	71.4%	75%	80%
SMA	50%	35.7%	-	20.3%

Fibroblastic & myofibroblastic tumors

In our study, fibroblastic & myofibroblastic tumors were the third most common tumors. This finding was similar to the findings of *shameera begum et al*[174] while these were fourth most common tumors in the study done by *Agravat et al.*[15] The benign tumors in this category included one case each of fibroma, angiofibroma and nodular fasciitis. Cases of both angiofibroma and fibroma occurred in upper limb while nodular fasciitis was seen in upper back region, in our study.*Agravat et al* [15] also found the cases of fibroma to be occurring in upper limb most commonly.

Fibromatosis [n=7] and solitary fibrous tumors [n=7] were the 2 common tumors diagnosed under the intermediate category. Fibromatosis had a widespread distribution while SFT was seen more commonly as abdominal wall and chest & mediastinal mass. Similary, *Jensen* [192] found palm [n=29] to be the most commonly affected site by fibromatosis followed by foot [n=14] and abdomen [n=5], out of 140 cases of fibroblastic tumors included in their study. However, *Stojandinovic et al* [193] conducted a study on 85 soft tissue tumors of the abdominal wall, out which desmoid fibromatosis [39 cases] was the commonest. All the cases of fibromatosis showed 100% nuclear positivity for beta-catenin, in our study. This finding isconsistent with study done by *Dorota E. et al.*[194] All the cases of solitary fibrous tumors showed 100% positivity for vimentin, CD34, Bcl2 and CD 99. While in the study done by *Nagarjun Rao et al*[195],

these markers showed positivity of 71.5%, 85%, 91% and 75% respectively.

The next common group of tumors in this category was DFSP [n=6]. Diagnosis of DFSP is usually made on histological features (storiform arrangement of spindle cells) but IHC is helpful when dealing with atypical features or with needle biopsies. All the 6 cases were consistently positive for CD34 which is a usual marker to distinguish these tumors from benign fibrous histiocytomas which are usually negative for the same.

We diagnosed only one case of low grade myofibroblastic sarcoma. *Montogomery et al* [196] also found it to be rare tumor having predilection for extremeties and head & neck. However in our study, this case presented as abdominal wall mass.

Peripheral nerve sheath tumors

In the present study, PNSTs were the were the fifth most common tumors constituting 9.73% of all soft tissue tumors. Benign PNSTs were more common than MPNSTs. Benign neural tumors formed the majority, constituting 72.22% of cases [n=18] and only 5 cases were diagnosed as malignant peripheral nerve sheath tumors. Schwannoma was the commonest benign neural tumor [n=11] followed by neurofibroma [n=2]. This is in agreement with the study done by *Kim et al* [197] who studied 397 peripheral nerve sheath tumors. *Gabhane et al* [198] concluded the two most common benign PNSTs to be schwannoma and neurofibroma. However, *Agravat et al* [15], *kransdorf* [162] and *kim et al* [197] found neurofibromas to be the commonest benign peripheral nerve sheath tumors.

The majority of cases fell in the age group of 31- 40 years with a mean age of 42.8 years and maximum number of cases affected the extremities. In a study done by Sasidharan SV et al., a total of 11 cases of MPNST were documented with a wide age range of 17-85 years. They also found extremities to be the most common site. While in a study done on PNSTs by *Panduranga et al* [199,200], maximum number of cases were seen

between 21-30 years and they found head & neck to be the commonest involved site.

On IHC all the cases of PNSTs showed 100% positivity for S-100. Although S-100 was diffusely positive in benign PNSTs, it showed focal positivity in cases of MPNST. Similarly, *Sasidharan et al* [200] also found that benign PNSTs show 100% positivity for S-100. However out of the 2 cases of MPNST studied, one of the case was S-100 negative in their study.

Skeletal muscle tumors

Rhabdomyosarcomas comprised 5.41% of all mesenchymal tumors. Out of the 10 cases, 3 cases were of ERMS, 1 case each of alveolar RMS, pleomorphic RMS, spindle cell RMS and 4 cases of RMS which were not otherwise specified. Occurrence of skeletal muscle tumors as compared to other soft tissue sarcomas is quite low. Hare et al[201] opined that it is apparently due to the fact that striated muscle cells are completely differentiated and do not undergo cellular division in postnatal life as other tissues.

In the present study the maximum number of cases were seen in head & neck region and as abdominal masses. Majority of these occurred in first two decades of life. This observation is similar to the studies of *Hare et al*[201] and *kransdorf* [162] who also observed head & neck to be the most common site and were seen commonly in first two decades of life. *Makino*[202] in his study on 23 cases of soft tissue tumors in head & neck region, found the highest incidence of RMS at this site [n=7].

On IHC, all the cases of RMS were 100% positive for vimentin, desmin and myogenin. Myogenin belongs to a group of myogenic regulatory proteins whose expression determines commitment and differentiation of primitive mesenchymal cells into skeletal muscle as observed by *Kumar et al*[203] and *Dodd et al.*[204] Thus, expression of myogenin has been demonstrated to be extremely specific for rhabdomyoblastic differentiation,

making it a useful marker in the differential diagnosis of RMS from other malignant small round cell tumors.

Adipocytic tumors

Adipocytic tumors are one of the most commonly occurring soft tissue tumors. Lipoma being the commonest tumor and is easily diagnosed on histological examination. However, in our study, only 9 cases were included, in which IHC was applied. Out of these, 8 cases were of liposarcoma and only 1 case of benign adipocytic tumor was seen. Male preponderance was seen with a male to female ratio of 3.5:1. However, *Agravat et al*[15] found a female predilection, while *Singh et al*[180] did not observe any sex predilection in these tumors.

In the present study, maximum number of cases were observed in the 6thand 8th decade. Similary, *Revathy et al* [205] also found these tumors to be occuring most commonly in 6th decade. However, *Shameera begum et al* [174] found 3rd, 4th and 5th decades to be the commonest affected age groups.

Lower limb (n=3) was found to be the most common site affected by these group of tumors followed by retroperitoneum(n=2) in the present study. This is in concordance with the finding of *kransdorf et al* [162] who also reported lower limb to be the commonest site.*Lucas et al* [206] and *Weiss et al* [207] observed that the most common site of involvement of well differentiated liposarcomas was extremities*. Amhad et al* [208] and *stout et al* [16] also found lower limb to be the commonest site followed by retroperitoneum with majority of cases occurring in 4th to 6th decade of life. While, *Singh et al* [180] observed that retroperitoneum was the most common site involved in cases of liposarcoma followed by lower limb.

Immunohistochemically, MDM2 showed 100% positivity in cases of liposarcoma in which it was applied. However, *Pilotti et al* [209] and *Binh et al* [117] found 86% and 97% positivity respectively in cases of liposarcoma. In our study, the case of spindle cell lipoma was S-100 negative and strongly positive for CD34. One case of dedifferentiated liposarcoma also

came out to be S-100 negative. *Templeton SF et al* [210], in a study of four cases of spindle cell lipomas found all cases to be CD34 positive and negative for S-100. *Rekhi B et al* [211] observed S-100 to be negative in 5 out of 9 cases of dedifferentiated liposarcoma.

Tumors of uncertain differentiation

Tumors of uncertain differentiation constituted 12.43% [n=23] of all mesenchymal tumors. All of them were malignant and included 13 cases of synovial sarcoma, 8 cases of ES/PNET and 2 cases of pleomorphic sarcoma. The age ranged from 10-80 years because of ES/PNET affecting children and younger age groups. However, cases of synovial sarcoma & pleomorphic sarcoma were seen in adults and elderly. We observed a female preponderance in this category of tumors with male to female ratio of 1:1.5. Similarly *Hare et al* [201] and *Sim et al* [212] also found these tumors in adults. However, *Sim et al* [212] found a male predilection in their study.

The most common site for synovial sarcoma in our study was the lower limb, this was also observed by *Hare et al* [201] and *Sim et al.* [212] On immunohistochemistry, vimentin showed 100% positivity with CK and EMA showing 77.87% and 57.14% positivity. However, *Olsen et al* [213] postulated EMA to be the most sensitive marker (91%) and they observed CK positivity in 70% cases of synovial sarcoma. *Rekhi B et al* [211] observed vimentin, CK and EMA positivity to be 100%, 60% and 76.4% respectively.

We observed that ES/PNET affected the head & neck region most commonly. *Nandeesh et al* [214] also observed ES/PNET to be the most common round cell tumors occurring in head & neck region. Immunohistochemically, in our study all the cases showed 100% membranous positivity for CD99. *Olsen et al* [213] observed membranous staining for CD99 to be more specific for ES/PNET and observed the same in 78% of cases. Both the cases of pleomorphic sarcoma included in present study, were vimentin positive and cytokeratin negative. One of the

case showed weak positivity for SMA and the other showed weak and focal positivity for desmin.

Pericytic tumors

There were total 5 cases in this category. 2 cases were of glomus tumor arising from pericytes, 2 cases were of angioleiomyoma and 1 case of myopericytoma. All the cases showed no age predilection and were seen almost equally in males and females. Both cases of glomus tumor and only case of myopericytoma were seen in upper limb, while angioleiomyoma presented as nasal mass and other case was seen in lower limb. Similarly, *Kransdorf* [162] and *Singh et al* [180] found upper limb to be the commonest site for glomus tumors with no age predilection. *Fukomoto et al* [215] in his study on ten cases of myopericytoma observed it to be arising from the subcutis of extremities.

Immunohistochemically, the cases of glomus tumor and angioleiomyoma showed SMA and CD34 positivity while, myopericytoma additionally showed positivity for h-caldesmon. CD34 was negative in tumor cells in case of myopericytoma.

Vascular tumors

This category included one case each of angiosarcoma and epithelioid hemangioendothelioma. These are one of the rarest soft tissue neoplasms. Both these cases were seen in males in 8th decade of life.

On IHC they were positive for vimentin and CD34 while SMA, CK and S-100 were negative. *Miettinen et al* [43] and *Wick MR* [133] in their studies found CD34 to be variably positive in vascular sarcomas.

Endometrial stromal sarcoma

All the 3 cases of ESS included in the study were seen in females within the age group of 41-60 years. On immunohistochemistry, all cases showed immunoreactivity for CD10. They showed ER positivity but were negative for SMA, desmin and CD34. P G Chu et al [216] also found Cd10 expression in all of their 16 cases. They found ER positivity in 12 out of 16 cases.

Although histopathological examination is considered gold standard in the diagnosis of mesenchymal tumors, IHC is of immense value in arriving at a final diagnosis, specially when faced with a malignant spindle cell neoplasm of a tumor having pleomorphic morphology. It is of use in distinguishing ES/PNET or embryonal RMS from other round cell tumors like lymphoma or neuroblastoma. Although there are some IHC markers which are specific for a particular lineage of cells, these can come positive rarely in other tumors also. So it is the combination of morphology and judicious use of IHC markers which can help us to arrive at a final diagnosis.

SUMMARY AND CONCLUSION

This study was conducted in Dayanand Medical College and Hospital, Ludhiana, over a period of five years (July 2016- June 2021). A total of 185 histologically diagnosed mesenchymal tumors were examined with respect to their immunohistochemical findings.

The following features were highlighted in this study:

- During the study period a total of 442 cases of mesenchymal tumors were received for histopathological examination in our department. Out of these, 185 cases of immunohistochemically confirmed mesenchymal neoplasms were analyzed with respect to light microscopic and immunohistochemical findings.
- The age of patients in our study ranged from 2 years to 90 years, with a mean age of 48.3 years.
- Smooth muscle tumors formed the largest group constituting 48 cases [25.95%]. Gastrointestinal stromal tumors were the second most common comprising 36 cases [19.56%] followed by fibroblastic &myofibroblastic tumors constituting 27 cases [14.69 %].
- Amongst smooth muscle tumors, SMA & h-Caldesmon were the most sensitive markers in our study both showing 100% positivity in case of leiomyoma and 97.4% & 100% positivity respectively, in case of LMS. Desmin showed 75% and 58.8% positivity in case of leiomyoma and LMS respectively.
- DOG-1 and C-kit were consistently found to be positive in GIST in 100% and 93.4% cases respectively.
- Fibromatosis had a widespread distribution while SFT was seen more commonly as abdominal wall and chest & mediastinal mass.All the cases of fibromatosis showed 100% nuclear positivity for beta-catenin andthe cases of solitary fibrous tumors showed 100% positivity for vimentin, CD34, Bcl2 and CD 99.

- All the 6 cases of DFSP were consistently positive for CD34 which is a useful marker to distinguish these tumors from benign fibrous histiocytomas which are usually negative for the same.
- In the present study, PNSTs comprised 9.73% of all soft tissue tumors. Benign neural tumors formed the majority, constituting 72.22% of cases [n=18] and only 5 cases were diagnosed as malignant peripheral nerve sheath tumors.
- All the cases of PNSTs showed 100% positivity for S-100. Although S-100 was diffusely positive in benign PNSTs, it showed focal positivity in cases of MPNST.
- Rhabdomyosarcomas comprised 5.41% of all mesenchymal tumors. Out of the 10 cases, 3 cases were of ERMS, 1 case each of alveolar RMS, pleomorphic RMS, spindle cell RMS and 4 cases of RMS which were not otherwise specified.All the cases of RMS were 100% positive for vimentin, desmin and myogenin.
- Out of total 9 cases of adipocytic tumors, 8 cases were of liposarcoma and only 1 case of benign adipocytic tumor was seen. On IHC, MDM2 showed 100% positivity in cases of liposarcoma,the case of spindle cell lipoma was S-100 negative and strongly positive for CD34. One case of dedifferentiated liposarcoma included in the study, also came out to be S-100 negative.
- Tumors of uncertain differentiation constituted 12.43% [n=23] of all mesenchymal tumors. All of them were malignant and included 13 cases of synovial sarcoma, 8 cases of ES/PNET and 2 cases of pleomorphic sarcoma. In cases of synovial sarcoma, vimentin showed 100% positivity with CK and EMA showing 77.87% and 57.14% positivity respectively.
- All the cases of ES/PNET showed 100% membranous positivity for CD99.Both the cases of pleomorphic sarcoma included in present study, were vimentin positive and cytokeratin negative. One of the case

showed weak positivity for SMA and the other showed weak and focal positivity for desmin.

- Amongst the pericytic tumors, the cases of glomus tumor and angioleiomyoma showed SMA and CD34 positivity while, myopericytoma showed positivity for h-caldesmon and was negative for CD34.
- Vascular tumors were positive for vimentin and CD34 while SMA, CK and S-100 were negative in these tumors.
- On IHC all the 3 cases of ESS showed immunoreactivity for CD10. They showed ER positivity but were negative for SMA, desmin and CD34.
- Although histopathological examination is considered gold standard in the diagnosis of mesenchymal tumors, IHC is of immense value in arriving at a final diagnosis.IHC markers which are specific for a particular lineage of cells, can rarely come positive in other tumors also. So it is the combination of morphology and judicious use of IHC markers which can help us to arrive at a final diagnosis.

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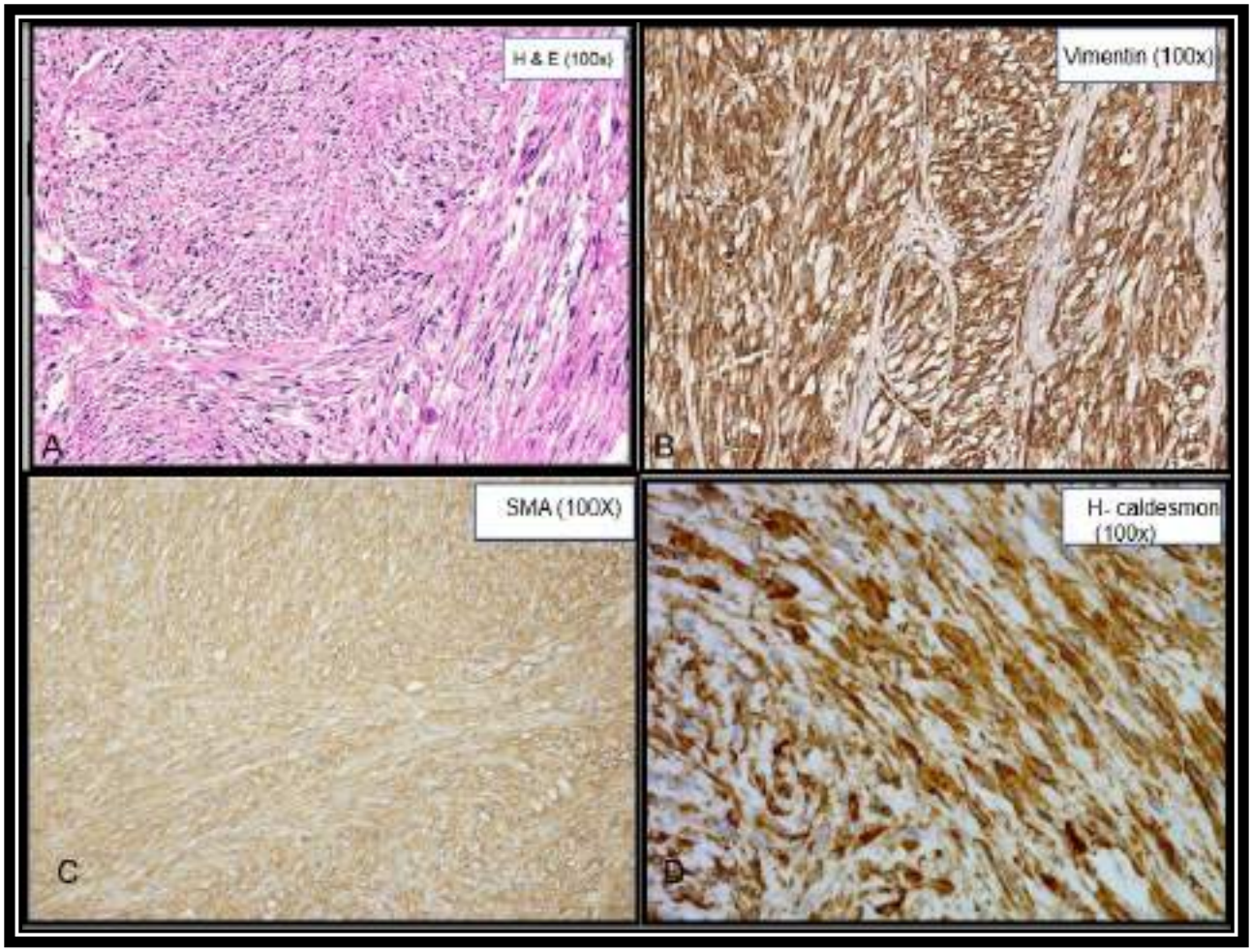
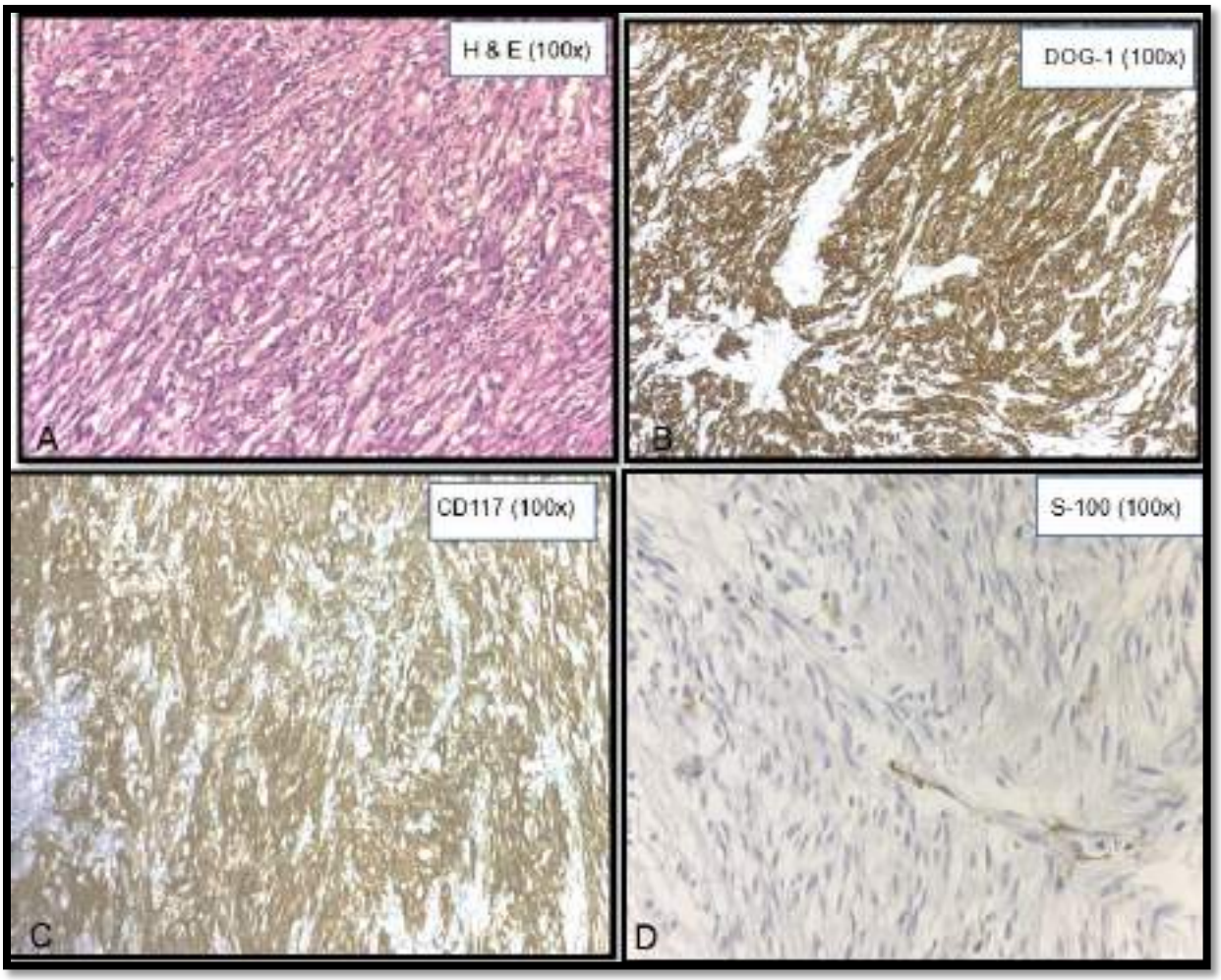
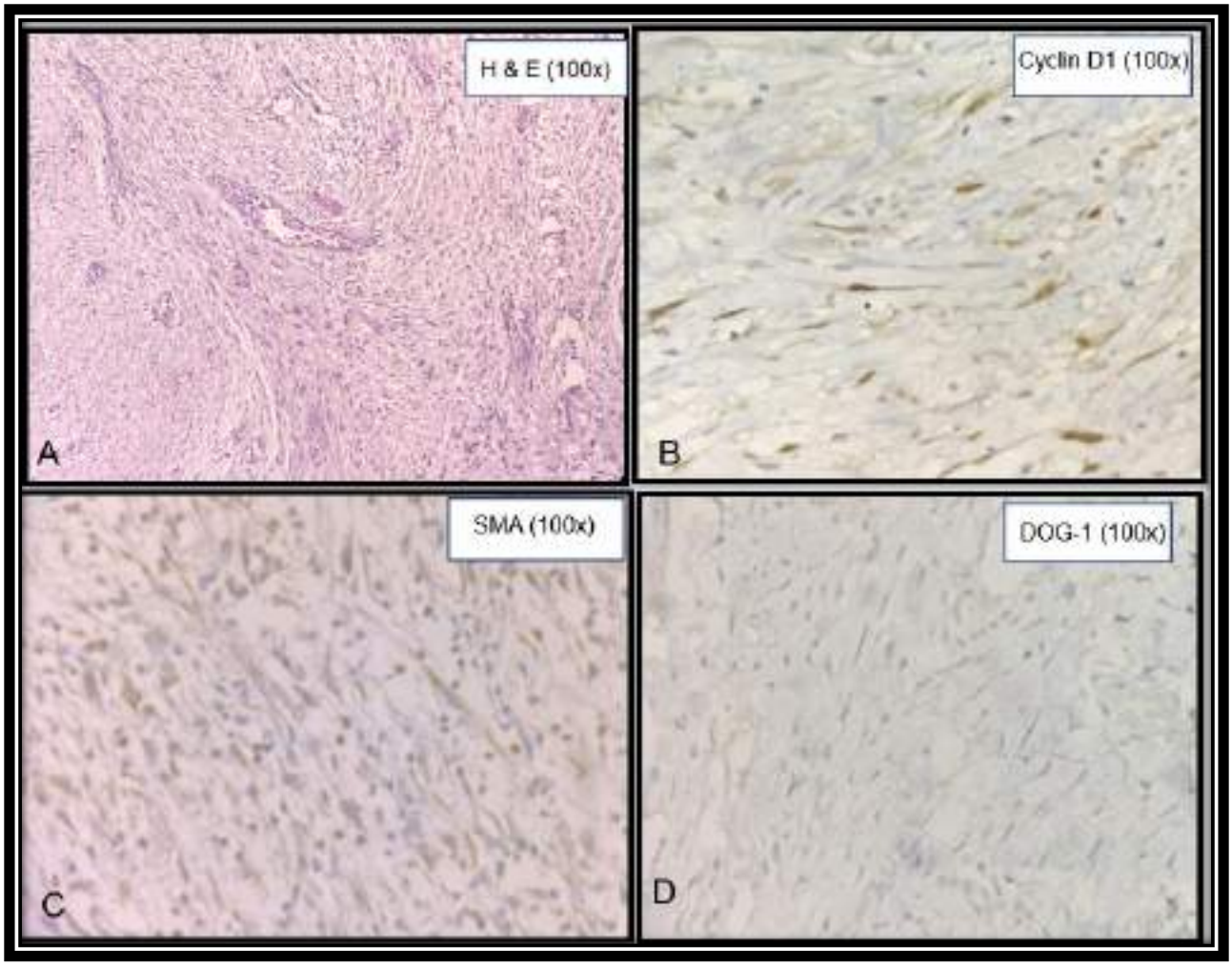


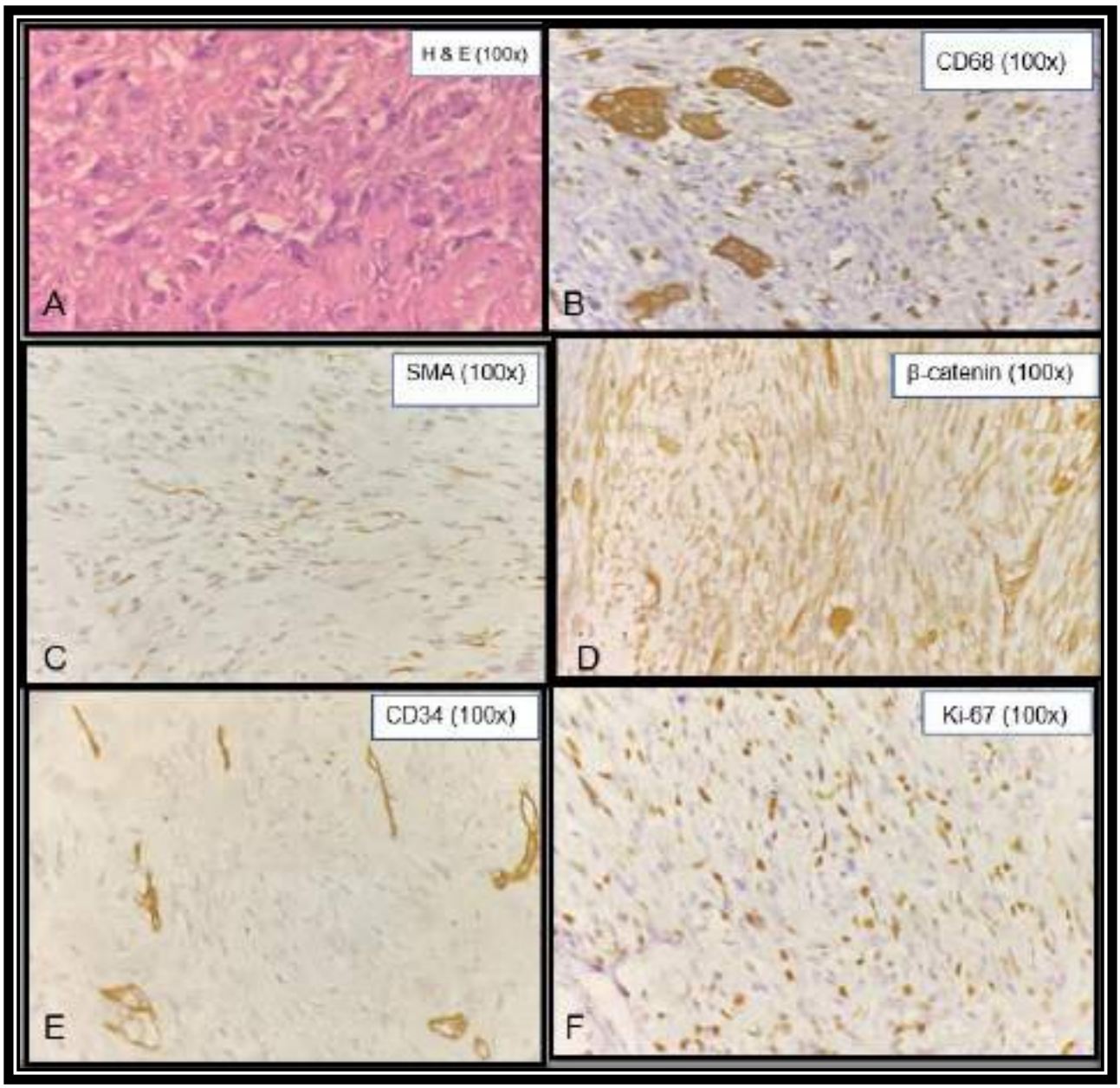
Picture 1: LEIOMYOSARCOMA: (A) Photomicrograph showing fascicles of spindle shaped cells exhibiting moderate nuclear pleomorphism, hyperchromasia and atypical mitotic figures (H&E,100x); on immunohistochemistry these cells are positive for (B,C,D) Vimentin, SMA, H-caldesmon (Cytoplasmic, 100x)



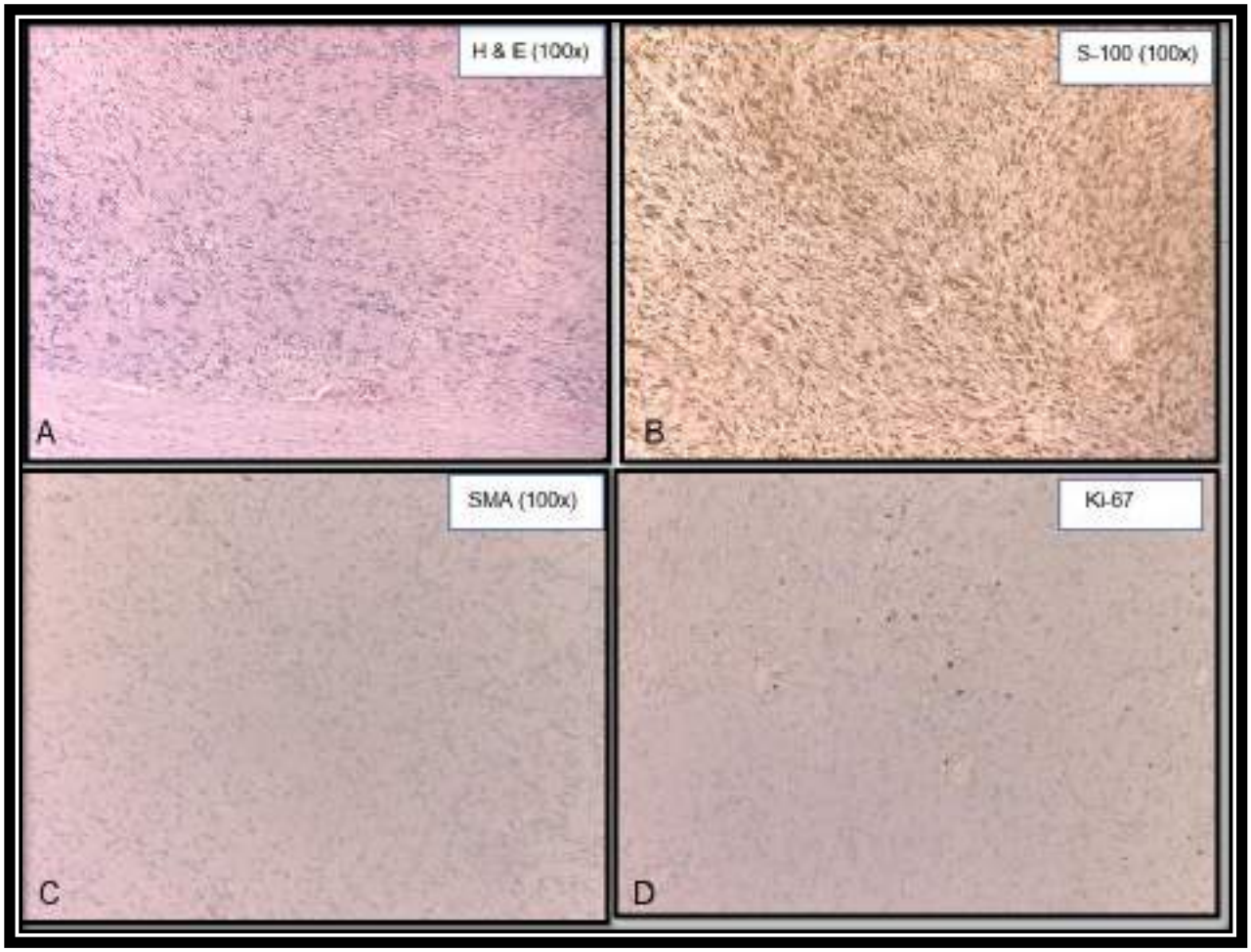
Picture 2: GASTROINTESTINAL STROMAL TUMOR: (A) Photomicrograph showing spindle cells in sheets with prominent paranuclear vacuoles (H&E, 100x); On immunohistochemistry tumor cells are positive for (B,C) DOG-1, CD117 (Membranous & cytoplasmic, 100x); (D) S-100 is negative in tumor cells (100x)



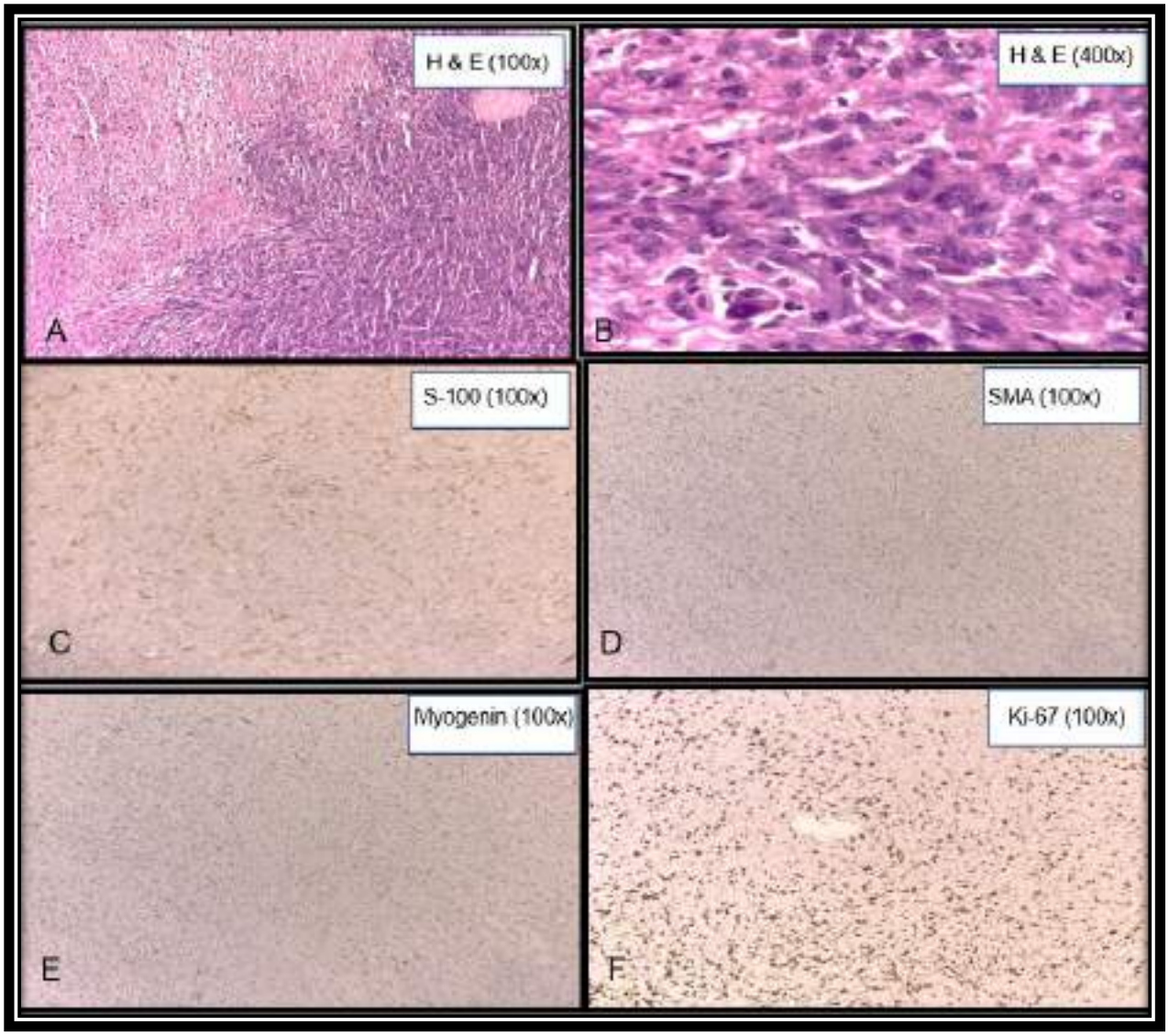
Picture 3: INFLAMMATORY MYOFIBROBLASTIC TUMOR: (A) Photomicrograph showing spindle shaped myofibroblastic cells admixed with inflammatory cells (H&E 100x); On immunohistochemistry lesional cells are positive for (B) Cyclin D1 (Nuclear, 100x), focal positive for (C) SMA (Cytoplasmic, 100x) and negative for (D) DOG-1 (100x)



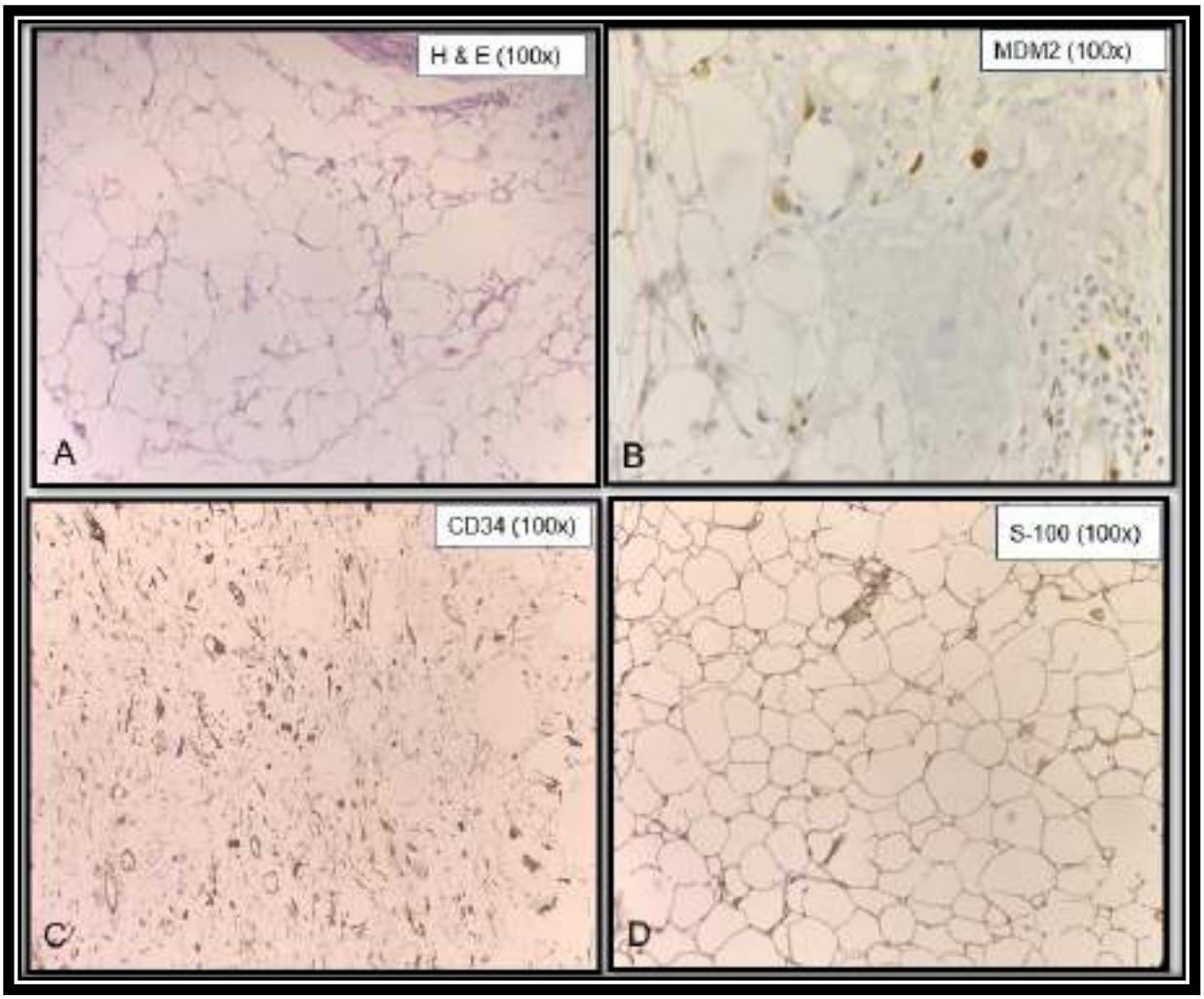
Picture 4: MALIGNANT FIBROUS HISTIOCYTOMA: (A) Photomicrograph showing pleomorphic areas consisting of spindle shaped cells admixed with histiocytes (H&E, 100x); On immunohistochemistry (B) CD68 is positive in giant cells (membranous& cytoplasmic, 100x), lesional cells are positive for (C,D) SMA, □-catenin (Cytoplasmic, 100x), (E) CD 34 is negative in lesional cells and highlights the blood vessels. (F) Ki-67 index is 35% in highest proliferating areas (Nuclear, 100x)



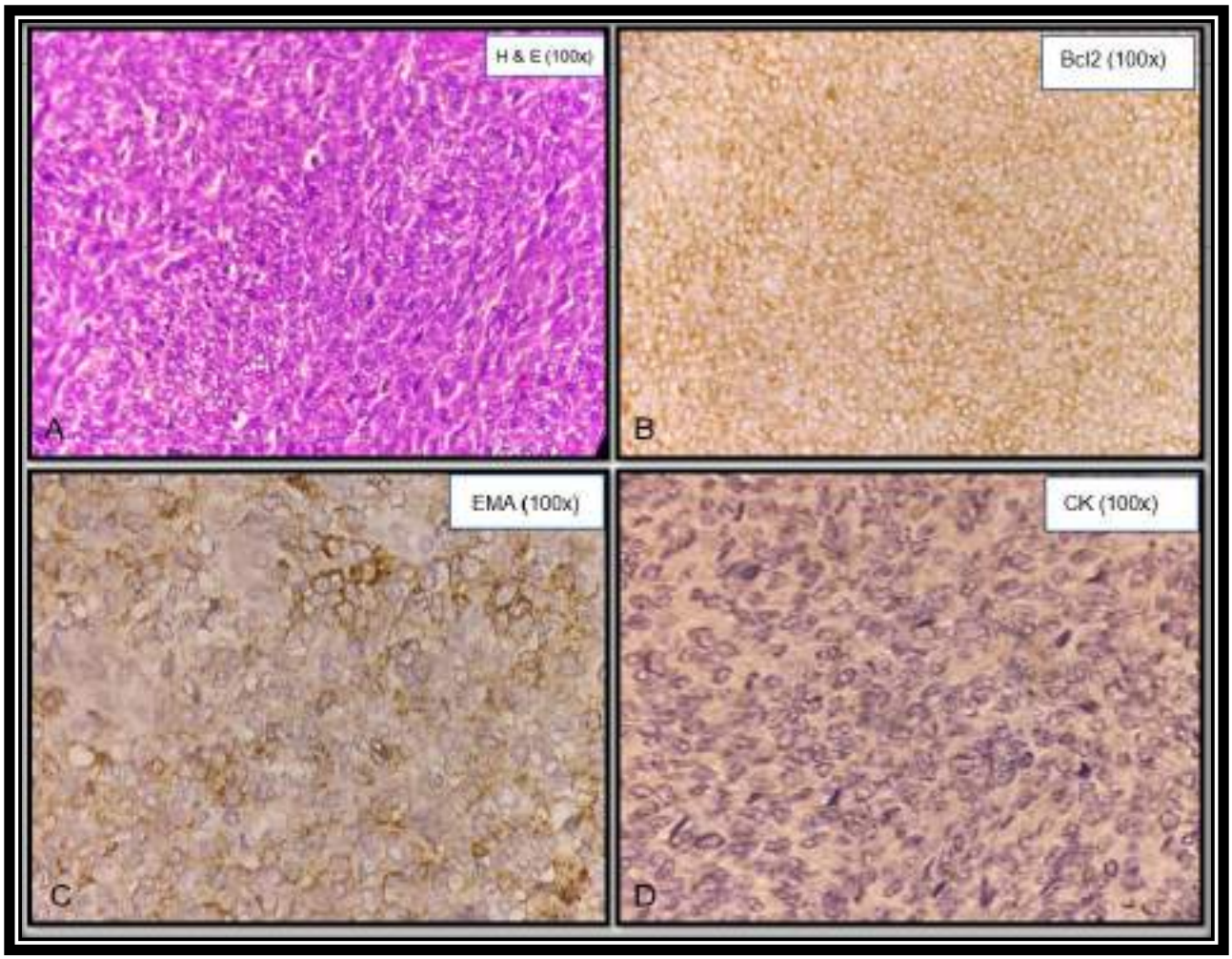
Picture 5: SCHWANNOMA: (A) Photomicrograph showing Antoni A and Antoni B areas (H&E, 100x); On immunohistochemistry tumor cells are diffuse strong positive for (B) S-100 (Cytoplasmic & nuclear, 100x), negative for (C) SMA (100x), (D) Ki-67 is 5% in highest proliferating areas (Nuclear, 100x).



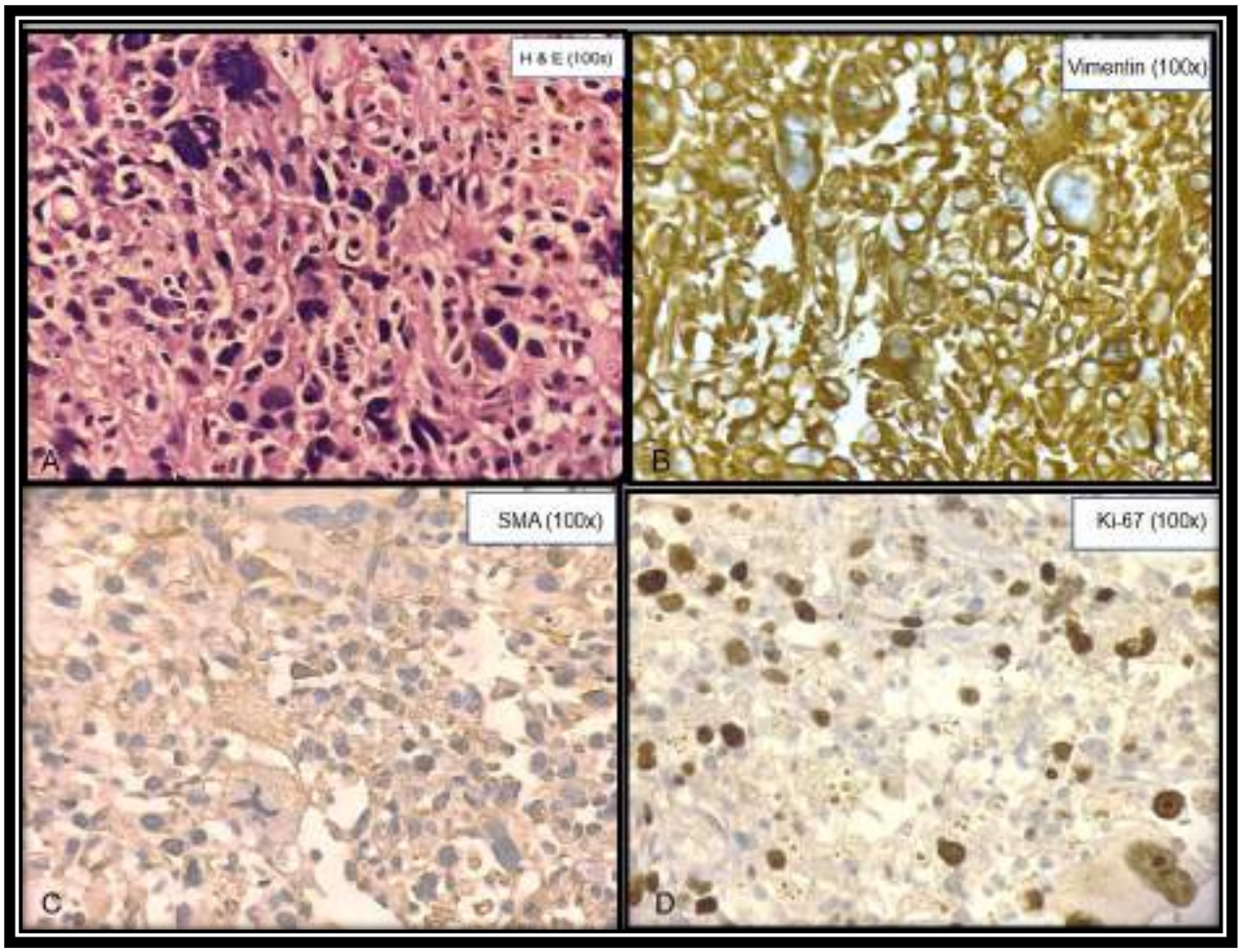
Picture 6: MALIGNANT PERIPHERAL NERVE SHEATH TUMOR: (A) Photomicrograph showing areas of necrosis and tumor cells in sheets (H&E, 100x), (B) spindle shaped tumor cells showing nuclear pleomorphism and hyperchromasia along with mitotic figures (H&E, 400x); On immunohistochemistry tumor cells are weak and focal positive for (C) S-100 (Cytoplasmic & nuclear, 100x) and negative for (D,E) SMA &Myogenin (100x), (F) Ki-67 is 60% in highest proliferating areas (Nuclear, 100x)



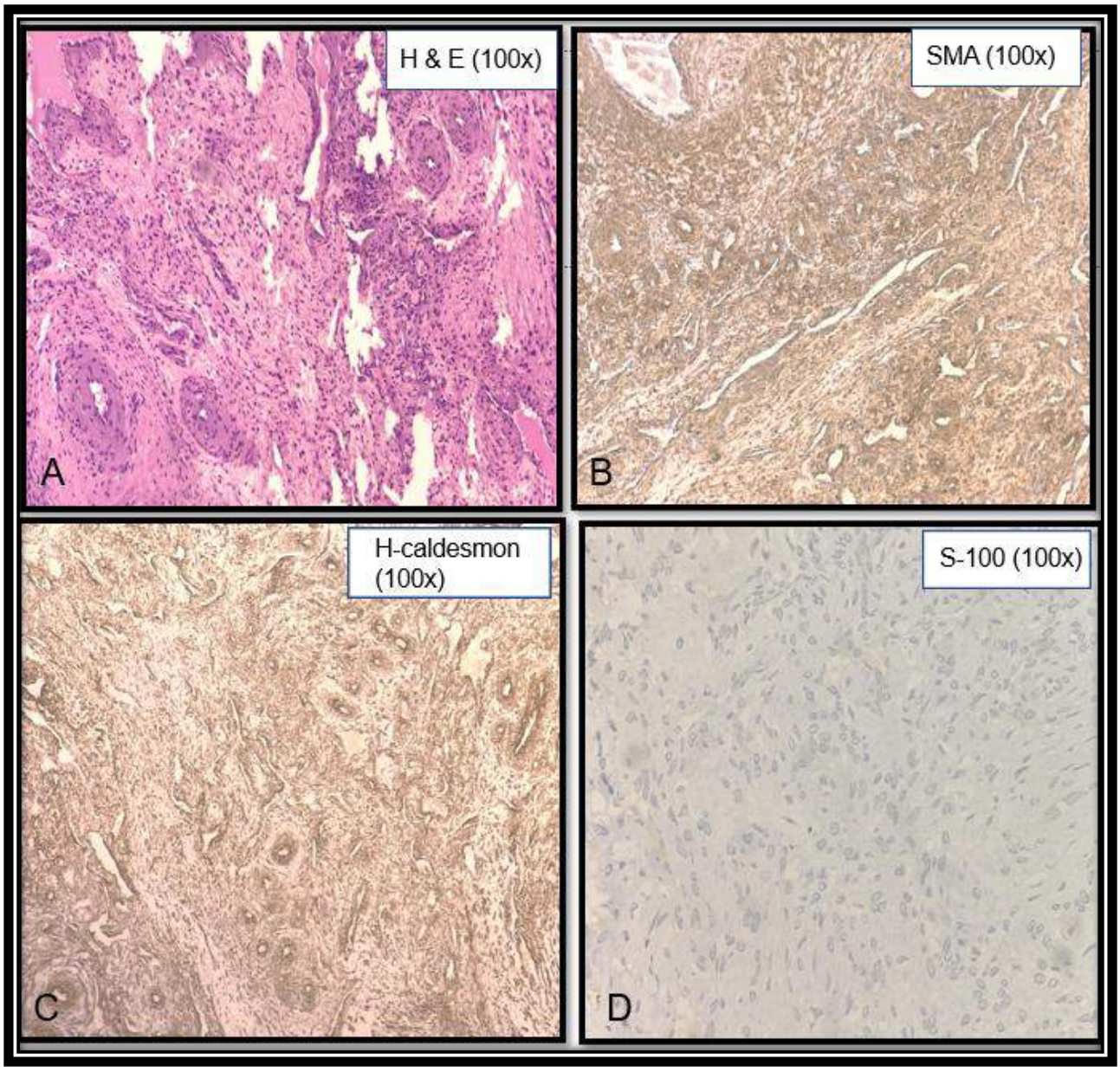
Picture 7: LIPOSARCOMA: (A) Photomicrograph showing varying sized adipocytes exhibiting nuclear atypia and hyperchromasia (H&E, 100x); On immunohistochemistry tumor cells are positive for (B,D) MDM2, S-100 (Cytoplasmic & nuclear, 100x) and positive for CD34 (Membranous, 100x)



Picture 8: SYNOVIAL SARCOMA (MONOPHASIC): (A) Photomicrograph showing monophasic spindle component having sheets of oval to spindle shaped cells (H&E, 100x); On immunohistochemistry tumor cells are positive for (B) Bcl2 (Cytoplasmic, 100x), Focal positive for (C) EMA (Cytoplasmic & membranous, 100x) and negative for (D) CK (100x).



Picture 9: PLEOMORPHIC SARCOMA: (A) Photomicrograph showing sheets of tumor cells exhibiting marked nuclear pleomorphism, hyperchromasia with many bizzare forms (H&E, 100x); On immunohistochemistry tumor cells are positive for (B) Vimentin (Cytoplasmic, 100x), weak focal positive for SMA (Cytoplasmic,100x) and Ki-67 is 50% in highest proliferating areas (Nuclear, 100x).



Picture 10: MYOPERICYTOMA: (A) Photomicrograph showing concentric perivascular whorled growth of spindle shaped cells (H&E, 100x); On immunohistochemistry tumor cells are positive for (B,C) SMA, H-caldesmon (Cytoplasmic, 100x) and negative for S-100 (100x)

Sr. No.	MRD No.	IHC No.	Sur. Path. No.	Initial name	Age	sex	Site of biopsy	Type of biopsy	Histological diagnosis	VIMENTIN	DESMIN	CYTOKERATIN	MYOGENIN	SMA	S-100	CD-34
1	101972	588-593/2016	6017/16	CR	55	FEMALE	BREAST	CORE BIOPSY	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	POSITIVE
2	123327	613-618/2016	7100/16	KK	50	FEMALE	UTERUS	EXCISIONAL	LEIOMYOMA	POSITIVE	POSITIVE		NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
3	117723	651-654/2016	6198/16	JK	47	FEMALE	BREAST	EXCISIONAL	MALIGNANT NEOPLASM ? METAPLASTIC CARCINOMA ?/ PHYLLOIDES TUMOR	POSITIVE	FOCAL POSITIVE			POSITIVE	NEGATIVE	
4	240811	699-703/2016	8410/16	MG	35	FEMALE	PLEURA	CORE BIOPSY	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE	NEGATIVE		NEGATIVE	NEGATIVE	NEGATIVE
5	113899	704-709/2016	5669/16	ALAMJIT	52	MALE	THIGH MASS	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE	POSITIVE			POSITIVE	NEGATIVE	NEGATIVE
6	93394	719-724/2016	8618/16	UR	61	FEMALE	PLEURA	CORE BIOPSY	SOLITARY FIBROUS TUMOR	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
7	135228	739-743/2016	8635/16	SS	36	MALE	CUBITAL FOSSA	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE			FOCAL POSITIVE	NEGATIVE	NEGATIVE
8	95379	800-806/2016	9193/16	KK	4	FEMALE	RIGHT UPPER LIP	CORE BIOPSY	ROUND CELL TUMOR	FOCAL POSITIVE	POSITIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE
9	139841	843-848/2016	9273/16	KK	42	FEMALE	LEFT ARM SWELLING			POSITIVE				FOCAL POSITIVE	NEGATIVE	NEGATIVE
10	116993	632-634,636/2016	6155/16	GD	60	MALE	THIGH MASS	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE		NEGATIVE		POSITIVE	NEGATIVE	NEGATIVE
11	337370	607/2017	10159/17	PK	30	FEMALE	PARASPINAL MASS	CORE BIOPSY	MESENCHYMAL TUMOR	POSITIVE	WEAK POSITIVE			NEGATIVE	POSITIVE	NEGATIVE
12	335349	594/2017	9964/17	YS	2	MALE	ABDOMINAL MASS	EXCISIONAL	MALIGNANT ROUND CELL TUMOR	POSITIVE	POSITIVE		POSITIVE	FOCAL POSITIVE	NEGATIVE	POSITIVE
13	326406	575/2017	9752/17	SS	75	MALE	OMENTAL BIOPSY	CORE BIOPSY	MALIGNANT ROUND CELL TUMOR			NEGATIVE	POSITIVE			
14	287456	486/2017	7394/17	HS	11	MALE	PLEURAL TISSUE	CORE BIOPSY	MALIGNANT ROUND CELL TUMOR	POSITIVE	POSITIVE	NEGATIVE	POSITIVE			
15	256475	371/2017	4760/17	GO	3	MALE	NECK SWELLING	CORE BIOPSY	MALIGNANT ROUND CELL TUMOR	POSITIVE	POSITIVE		POSITIVE			
16	388619	752/2017	13214/17	NK	63	MALE	LEFT INGUINAL SWELLING	EXCISIONAL	SPINDLE CELL LIPOMA	POSITIVE	POSITIVE			NEGATIVE	NEGATIVE	POSITIVE
17	300231	747/2017	13184/17	KAMALDEEP	18	FEMALE	LEFT FEMUR	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			POSITIVE	NEGATIVE	NEGATIVE
18	368554	726/2017	12562/17	AC	47	MALE	ANTERIOR ABDOMINAL WALL	EXCISIONAL		POSITIVE	POSITIVE			NEGATIVE	NEGATIVE	POSITIVE
19	293736	657/2017	11272/17	NS	58	MALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			POSITIVE	NEGATIVE	POSITIVE
20	330327	583,642/2017	9506,10486/17	BK	36	FEMALE	ESOPHAGEAL MASS	EXCISIONAL	BENIGN NEUROGENIC TUMOR	POSITIVE	FOCAL POSITIVE			NEGATIVE	POSITIVE	NEGATIVE
21	329144	611/2017	9756/17	SP	65	FEMALE	RETROPERITONEAL MASS	EXCISIONAL		POSITIVE	POSITIVE	FOCAL POSITIVE	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE
22	337842	613/2017	10129/17	DS	70	MALE	RETROPERITONEAL MASS	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	POSITIVE		NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
23	329644	606/2017	10155/17	LS	72	FEMALE	UTERUS	EXCISIONAL	MESENCHYMAL TUMOR-LEIOMYOSARCOMA		NEGATIVE			POSITIVE		NEGATIVE
24	313289	544/2017	8748/17	KALPANA	40	FEMALE	UTERUS	EXCISIONAL	MESENCHYMAL TUMOR -LEIOMYOSARCOMA	POSITIVE	POSITIVE					NEGATIVE
25	297721	591/2017	9852/17	VK	57	MALE	THIGH MASS			POSITIVE	NEGATIVE		NEGATIVE	FOCALLY POSITIVE	NEGATIVE	NEGATIVE
26	329217	573/2017	9703/17	DS	70	MALE	NASAL SWELLING	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			POSITIVE		POSITIVE
27	328053	579/2017	9569/17	PK	28	MALE	RETROPERITONEAL MASS	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE	FOCAL POSITIVE			FOCAL POSITIVE	NEGATIVE	NEGATIVE
28	324492	550/2017	9197/17	GK	46	FEMALE	JEJUNAL MASS	EXCISIONAL	SPINDLE CELL TUMOR		NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
29	287264	499/2017	7249/17	RK	36	FEMALE	CHEST WALL SWELLING	CORE BIOPSY	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	OCCASIONAL FOCAL POSITIVE
30	283666	483/2017	6610/17	AS	72	MALE	LEFT PLEURA	CORE BIOPSY	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
31	38323	432/2017	5576/17	YS	24	MALE	RIGHT HAND	EXCISIONAL	SPINDLE CELL LESION ? FIBROMATOSIS	POSITIVE	POSITIVE		NEGATIVE	FOCAL POSITIVE	NEGATIVE	NEGATIVE
32	265661	426/2017	5336/17	ANUREETA	42	FEMALE	RETROPERITONEAL MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	POSITIVE		NEGATIVE	POSITIVE	NEGATIVE	WEAK FOCAL POSITIVE
33	272312	413/2017	5699/17	AD	53	FEMALE	RETROPERITONEAL MASS			POSITIVE	FOCAL POSITIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE
34	255666	379/2017	4592/17	HITESH	17	MALE	LEG MASS	EXCISIONAL	BENIGN NEUROGENIC TUMOR-SCHWANOMMA	POSITIVE	NEGATIVE			FOCAL POSITIVE	POSITIVE	NEGATIVE
35	242672	362/2017	3771/17	SA	20	MALE	POSTERIOR KNEE MASS	EXCISIONAL		POSITIVE			NEGATIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE
36	249176	361/2017	4252/17	MK	15	FEMALE	RIGHT LEG MASS	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			NEGATIVE	POSITIVE	NEGATIVE
37	236584	338/2017	3415/17	RAJINDER	58	MALE	THIGH MASS	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE	POSITIVE		NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
38	194849	315/2017	1567/17	RAJWANT	36	MALE	NECK SWELLING	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE			NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE
39	199172	268/2017	1038/17	HARJINDER	55	MALE	RIGHT THIGH MASS	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE		NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
40	393388	778/2017	13604/17	USHA	61	FEMALE	RIGHT KNEE MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR		POSITIVE	FOCAL POSITIVE IN EPITHELIAL COMPONENT		NEGATIVE	NEGATIVE	NEGATIVE
41	273925	430/2017	5875/17	JASREET	2	FEMALE	RIGHT MANDIBULAR MASS	EXCISIONAL	MALIGNANT ROUND CELL TUMOR	FOCAL POSITIVE						NEGATIVE
42	221863	295/2017	2654/17	JS	19	MALE	NECK MASS	EXCISIONAL	MALIGNANT ROUND CELL TUMOR	POSITIVE	POSITIVE		NEGATIVE	NEGATIVE		
43	412545	37/2018	255/18	SS	31	MALE	JEJUNAL GROWTH	EXCISIONAL	MESENCHYMAL TUMOR		NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
44	418579	38/2018	296/18	SK	30	FEMALE	RECTUS SHEATH MASS	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR LIKELY FIBROMATOSIS	POSITIVE	NEGATIVE			FOCAL POSITIVE	NEGATIVE	NEGATIVE
45	429431	71/2018	1258/18	RAJESH	49	MALE	RIGHT LOWER LIMB MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	POSITIVE	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
46	431378	74/2018	1367/18	SUKHDEV	23	MALE	OLFACTORY GROOVE TISSUE	INCISIONAL	HIGH GRADE MALIGNANT TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE			
47	435780	92/2018	1602/18	AD	65	MALE	STOMACH	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR LIKELY FIBROMATOSIS	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
48	436106	93/2018	1653/18	TD	85	FEMALE	INTRAMURAL JEJUNAL MASS	EXCISIONAL	SPINDLE CELL LESION	POSITIVE	NEGATIVE			POSITIVE	NEGATIVE	POSITIVE
49	424915	103/2018	929/18	SS	68	MALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE				NEGATIVE	NEGATIVE	
50	388973	112/2018	1815/18	NIRMALA	65	FEMALE	RIGHT LUNG	CORE BIOPSY	SPINDLE CELL TUMOR	POSITIVE		NEGATIVE		NEGATIVE	NEGATIVE	POSITIVE

Sr. No.	MRD No.	Bcl-2	C-KIT	DOG-1	EMA	CD-99	WT-1	SYNAPTOPHYSIN	CHROMOGRANIN A	Tdt	CD-3	CD-7	PAX-5	LCA(CD45)	HMB 45	CD-10	BETA CATENIN	ER	PR	CD-68
1	101972																			
2	123327																			
3	117723																			
4	240811	POSITIVE																		
5	113899		POSITIVE																	
6	93394	FOCAL POSITIVE																		
7	135228																			
8	95379																			
9	139841																			
10	116993		NEGATIVE	NEGATIVE																
11	337370		NEGATIVE																	
12	335349				NEGATIVE	POSITIVE	POSITIVE	NEGATIVE												
13	326406					FOCAL POSITIVE		NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE						
14	287456					FOCAL POSITIVE		NEGATIVE	NEGATIVE					NEGATIVE						
15	256475													NEGATIVE						
16	388619	NEGATIVE																		
17	300231																			
18	368554					POSITIVE														
19	293736		POSITIVE																	
20	330327		NEGATIVE																	
21	329144				NEGATIVE										NEGATIVE					
22	337842				NEGATIVE															
23	329644						POSITIVE									NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	
24	313289		NEGATIVE																	
25	297721				FOCAL POSITIVE												NEGATIVE			
26	329217														NEGATIVE					
27	328053																			
28	324492		POSITIVE																	
29	287264		NEGATIVE														NEGATIVE	NEGATIVE		NEGATIVE
30	283666	POSITIVE																		
31	38323	NEGATIVE	NEGATIVE		NEGATIVE												POSITIVE			
32	265661	NEGATIVE	NEGATIVE																	
33	272312	NEGATIVE	FOCAL POSITIVE																	
34	255666																			
35	242672	POSITIVE																		
36	249176	NEGATIVE																		
37	236584	NEGATIVE																		
38	194849		NEGATIVE																	
39	199172																			
40	393388				POSITIVE															
41	273925					POSITIVE			FOCAL DOT LIKE					NEGATIVE		NEGATIVE				
42	221863					POSITIVE		NEGATIVE	NEGATIVE					NEGATIVE						
43	412545		POSITIVE																	
44	418579		NEGATIVE														POSITIVE			
45	429431	NEGATIVE				FOCAL POSITIVE											POSITIVE			
46	431378				NEGATIVE	POSITIVE		NEGATIVE	NEGATIVE	NEGATIVE				NEGATIVE						
47	435780		POSITIVE			FOCAL POSITIVE														
48	436106		POSITIVE			FOCAL POSITIVE														
49	424915		POSITIVE																	
50	388973				NEGATIVE	POSITIVE														

Sr. No.	MRD No.	P63	CK-7	CK-20	CALRETININ	INHIBIN A	GFAP	TTF-1	CK8/18	P16	P53	CD63	MDM2	H-CALDESMON	CD20	ALK-1	NSE	PAX 8	CYCLIN D1	MIB-1 (%)	FINAL IHC DIAGNOSIS
1	101972																				LEIOMYOSARCOMA
2	123327																				LEIOMYOMA
3	117723																				LEIOMYOSARCOMA
4	240811																				MONOPHASIC SYNOVIAL SARCOMA
5	113899																			1	LEIOMYOMA
6	93394																				SOLITARY FIBROUS TUMOR
7	135228																				LEIOMYOMA
8	95379																				RHABDOMYOSARCOMA
9	139841																				MALIGNANT FIBROUS HISTIOCYTOMA
10	116993																				LEIOMYOSARCOMA
11	337370																			1	SCHWANNOMA
12	335349																			50	RHABDOMYOSARCOMA
13	326406																			60	RHABDOMYOSARCOMA
14	287456																			50	RHABDOMYOSARCOMA
15	256475																				RHABDOMYOSARCOMA
16	388619																			<1	SPINDLE CELL LIPOMA
17	300231													POSITIVE						5	LEIOMYOSARCOMA
18	368554																			5	DERMATOFIBROSARCOMA PROTUBERANS
19	293736																			3	GASTROINTESTINAL STROMAL TUMOR
20	330327																			2	SCHWANNOMA
21	329144																				RHABDOMYOSARCOMA
22	337842																			45	LEIOMYOSARCOMA
23	329644																				LEIOMYOSARCOMA
24	313289																			12	LEIOMYOSARCOMA
25	297721																			20	FIBROMYXOID SARCOMA
26	329217																			2	ANGIOLEIOMYOMA
27	328053																			18	LEIOMYOSARCOMA
28	324492																			3	GASTROINTESTINAL STROMAL TUMOR
29	287264																			50	LEIOMYOSARCOMA
30	283666																				SOLITARY FIBROUS TUMOR
31	38323					NEGATIVE														1	FIBROMATOSIS
32	265661																			60	LEIOMYOSARCOMA
33	272312																			90	RHABDOMYOSARCOMA
34	255666																			8	SCHWANNOMA
35	242672		FOCAL POSITIVE																	10	SYNOVIAL SARCOMA
36	249176																			35	MALIGNANT PERIPHERAL NERVE SHEATH TUMOR
37	236584																			35	LEIOMYOSARCOMA
38	194849																			25	MALIGNANT PERIPHERAL NERVE SHEATH TUMOR
39	199172																			10	LEIOMYOSARCOMA
40	393388		NEGATIVE					NEGATIVE												15	SYNOVIAL SARCOMA
41	273925						NEGATIVE													90	EWING'S SARCOMA/PNET
42	221863																			50	EWING'S SARCOMA/PNET
43	412545																			3	GASTROINTESTINAL STROMAL TUMOR
44	418579																			<1	FIBROMATOSIS
45	429431																			25	LEIOMYOSARCOMA
46	431378						NEGATIVE													70	EWING'S SARCOMA/PNET
47	435780																			55	GASTROINTESTINAL STROMAL TUMOR
48	436106																			1	GASTROINTESTINAL STROMAL TUMOR
49	424915																			2	GASTROINTESTINAL STROMAL TUMOR
50	388973		NEGATIVE	NEGATIVE	NEGATIVE																SOLITARY FIBROUS TUMOR

Sr. No.	MRD No.	IHC No.	Sur. Path. No.	Initial name	Age	sex	Site of biopsy	Type of biopsy	Histological diagnosis	VIMENTIN	DESMIN	CYTOKERATIN	MYOGENIN	SMA	S-100	CD-34
51	455294	123/2018	2699/18	PARAMJEET	35	FEMALE	TUBOOVARIAN MASS	CORE BIOPSY	SPINDLE CELL NEOPLASM POSSIBLY LEIOMYOMA	POSITIVE	POSITIVE			POSITIVE	NEGATIVE	NEGATIVE
52	452123	134/2018	2500/18	GS	56	MALE	PROXIMAL JEJUNAL MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE		NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
53	458843	144/2018	2988/18	MANJIT	16	MALE	BRAIN	EXCISIONAL	MALIGNANT ROUND SMALL CELL TUMOR ? EWING'S SARCOMA/PNET			NEGATIVE				
54	467180	150/2018	3511/18	AS	7	MALE	RIGHT LUNG	CORE BIOPSY	MALIGNANT ROUND CELL TUMOR	FOCAL POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE			
55	459058	163/2018	3543/18	SHWETA	27	FEMALE	RIGHT KNEE MASS	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE		NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
56	464296	171/2018	3671/18	GURBAX	60	MALE	TESTICULAR MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	WEAK POSITIVE	NEGATIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	NEGATIVE
57	474600	200/2018	4040/18	SS	42	MALE	LEFT RETROPERITONEAL MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR WITH PROMINENT MYXOID CHANGE	POSITIVE				NEGATIVE	POSITIVE IN ADIPOCYTES	POSITIVE
58	489805	216/2018	5112/18	NITYA	15	FEMALE	RIGHT SHOULDER MASS	CORE BIOPSY	SPINDLE CELL MESENCHYMAL TUMOR					NEGATIVE	NEGATIVE	NEGATIVE
59	475490	221/2018	4416/18	SS	71	MALE	SOFT TISSUE MASS ON BACK	EXCISIONAL	SPINDLE CELL LESION POSSIBLY FIBROMATOSIS	POSITIVE	NEGATIVE		POSITIVE	POSITIVE	NEGATIVE	NEGATIVE
60	487546	244/2018	5223/18	DK	51	FEMALE	ESOPHAGEAL MASS	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR	POSITIVE				NEGATIVE	POSITIVE	NEGATIVE
61	497692	259/2018	5672/18	RK	58	FEMALE	THIGH MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	POSITIVE IN EPITHELIAL COMPONENT	NEGATIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE
62	148733	262/2018	6141/18	SG	54	FEMALE	PELVIC MASS	CORE BIOPSY	SPINDLE CELL MESENCHYMAL TUMOR	POSITIVE			NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
63	507844	314/2018	6745/18	DK	61	MALE	ANTERIOR ABDOMINAL WALL	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE				NEGATIVE	NEGATIVE	POSITIVE
64	81273	329/2018	7255/18	ANITA	41	FEMALE	LEFT VASTUS LATERALIS	EXCISIONAL	MALIGNANT SPINDLE CELL SARCOMA	POSITIVE	NEGATIVE	POSITIVE IN EPITHELIAL COMPONENT	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
65	522160	330/2018	7432/18	AK	50	FEMALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE		NEGATIVE		NEGATIVE	NEGATIVE	POSITIVE
66	440563	355/2018	6538/18	KP	40	FEMALE	TUBOOVARIAN MASS	EXCISIONAL	BENIGN MESENCHYMAL TUMOR POSSIBLY LEIOMYOMA		POSITIVE			POSITIVE	NEGATIVE	
67	552125	413/2018	9533/18	SJ	22	FEMALE	LEFT CALF LESION	EXCISIONAL	SPINDLE CELL NEOPLAM ? NEUROGENIC ? MYOFIBROMA	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	FOCAL POSITIVE
68	543416	420/2018	9095/18	REKHA	45	FEMALE	UTERUS	EXCISIONAL	ENDOMETRIAL STROMAL SARCOMA			NEGATIVE		NEGATIVE	NEGATIVE	NEGATIVE
69	556253	430/2018	9876/18	SK	50	FEMALE	ABDOMINAL MASS	CORE BIOPSY	MESENCHYMAL TUMOR ? SMOOTH MUSCLE IN ORIGIN		NEGATIVE			NEGATIVE	FOCAL POSITIVE	
70	571124	528/2018	11275/18	SAZIA	25	FEMALE	SMALL INTESTINE	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			POSITIVE	NEGATIVE	POSITIVE
71	572242	537/2018	10929/18	KS	58	MALE	NODULE AT BACK	INCISIONAL	MESENCHYMAL NEOPLASM	POSITIVE	NEGATIVE			FOCAL POSITIVE	NEGATIVE	NEGATIVE
72	591261	543/2018	12297/18	GS	58	MALE	STOMACH	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
73	592438	555/2018	12354/18	SUSHMA	58	FEMALE	STOMACH	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR					NEGATIVE	NEGATIVE	POSITIVE
74	596204	559/2018	12552/18	PARNOOR	15	FEMALE	RIGHT LEG MASS	EXCISIONAL	BENIGN NEUROGENIC TUMOR-NEUROFIBROMA	POSITIVE				NEGATIVE	POSITIVE	
75	565720	573/2018	10496/18	RM	48	FEMALE	EPIGASTRIC MASS	CORE BIOPSY	MESENCHYMAL TUMOR	POSITIVE		NEGATIVE		POSITIVE	NEGATIVE	NEGATIVE
76	609360	602/2018	13643/18	RK	45	FEMALE	INGUINAL MASS	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			NEGATIVE	FOCAL POSITIVE	NEGATIVE
77	238777	603/2018	115268/18	HK	71	FEMALE	ILIAC LYMPH NODE	CORE BIOPSY	SPINDLE CELL NEOPLASM	POSITIVE	FOCAL POSITIVE	NEGATIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	DIFFUSE POSITIVE
78	614698	614/2018	13722/18	KR	76	FEMALE	ABDOMINAL MASS	CORE BIOPSY	SPINDLE CELL MESENCHYMAL TUMOR	POSITIVE	POSITIVE			POSITIVE	NEGATIVE	NEGATIVE
79	611649	636/2018	13638/18	SC	63	MALE	DUODENAL BIOPSY	INCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	NEGATIVE		NEGATIVE	NEGATIVE	FOCAL POSITIVE
80	634063	670/2018	14962/18	GS	74	FEMALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	FOCAL POSITIVE			POSITIVE	NEGATIVE	NEGATIVE
81	610681	677/2018	15070/18	KL	66	FEMALE	STOMACH	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
82	638843	689/2018	15447/18	DS	63	MALE	RECTAL MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	POSITIVE	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
83	744829	431/2019	7313/19	SK	58	FEMALE	THIGH MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE		NEGATIVE	WEAK POSITIVE	NEGATIVE	
84	643289	101/2019	15673/18	MS	78	MALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	FOCAL POSITIVE
85	642112	011/2019	15585/18	SARWAN	78	MALE	THIGH MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR		NEGATIVE	FOCAL POSITIVE		NEGATIVE	NEGATIVE	NEGATIVE
86	648578	19/2019	248/2019	AS	15	MALE	LYMPH NODE	CORE BIOPSY	MALIGNANT NEOPLASM	POSITIVE	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE
87	657908	64/2019	862/2019	PK	23	FEMALE	RIGHT INDEX FINGER	EXCISIONAL	GLOMUS TUMOR	POSITIVE		NEGATIVE		POSITIVE	NEGATIVE	POSITIVE
88	664643	77/2019	1297/2019	RS	40	MALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
89	665371	82/2019	1303/2019	AS	74	MALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			POSITIVE	NEGATIVE	POSITIVE
90	666679	91/2019	1424/2019	RD	61	FEMALE	THIGH MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	WEAK POSITIVE					NEGATIVE
91	674583	119/2019	1928/2019	JS	64	MALE	STOMACH	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE				POSITIVE	FOCAL POSITIVE	
92	669708	124/2019	1889/2019	DK	70	FEMALE	RIGHT HEPATECTOMY	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	NEGATIVE		NEGATIVE	NEGATIVE	POSITIVE
93	678585	128/2019	2333/2019	YASHPAL	52	MALE	THIGH MASS	CORE BIOPSY	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	NEGATIVE		POSITIVE	NEGATIVE	NEGATIVE
94	680181	144/2019	2331/2019	GS	48	MALE	JEJUNAL MASS	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE				NEGATIVE	POSITIVE	POSITIVE
95	679504	147/2019	2148/2019	AJ	66	MALE	LUMP RIGHT THIGH	CORE BIOPSY	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	POSITIVE
96	676775	154/2019	2020/2019	KG	39	FEMALE	UTERUS	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	POSITIVE			POSITIVE	NEGATIVE	NEGATIVE
97	688430	158/2019	2807/2019	SS	18	MALE	INTRAABDOMINAL MASS	CORE BIOPSY	SMALL ROUND CELL TUMOR	POSITIVE		NEGATIVE				
98	227263	313/2017	6611/2017	RANVIR	63	FEMALE	LEFT ARM SWELLING	INCISIONAL	SPINDLE CELL TUMOR	POSITIVE	FOCAL POSITIVE			NEGATIVE	NEGATIVE	POSITIVE
99	693791	176/2019	3086/2019	MK	35	MALE	BLOCKS FOR REVIEW	EXCISIONAL	DESMOID FIBROMATOSIS		FOCAL POSITIVE		NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
100	590437	177/2019	3032/2019	TS	28	FEMALE	SUBSEROSAL FIBROID	EXCISIONAL	SMOOTH MUSCLE TUMOR							

Sr. No.	MRD No.	Bcl-2	C-KIT	DOG-1	EMA	CD-99	WT-1	SYNAPTOPHYSIN	CHROMOGRANIN A	Tdt	CD-3	CD-7	PAX-5	LCA(CD45)	HMB 45	CD-10	BETA CATENIN	ER	PR	CD-68
51	455294		NEGATIVE																	
52	452123		NEGATIVE	NEGATIVE													CYTOPLASMIC POSITIVITY			
53	458843				FOCAL POSITIVE	POSITIVE		NEGATIVE	NEGATIVE					NEGATIVE						
54	467180					POSITIVE								NEGATIVE						
55	459058	POSITIVE															CYTOPLASMIC POSITIVITY			NEGATIVE
56	464296																CYTOPLASMIC POSITIVITY			POSITIVE IN GIANT CELLS
57	474600																			POSITIVE
58	489805	POSITIVE			NEGATIVE												POSITIVE			
59	475490																POSITIVE			
60	487546		NEGATIVE	NEGATIVE																
61	497692	POSITIVE															FOCAL CYTOPLASMIC			NEGATIVE
62	148733		NEGATIVE	NEGATIVE												NEGATIVE		NEGATIVE		
63	507844	NEGATIVE															NEGATIVE			NEGATIVE
64	81273	FOCAL POSITIVE			FOCAL POSITIVE												POSITIVE			
65	522160		POSITIVE	POSITIVE	NEGATIVE															
66	440563		NEGATIVE																	
67	552125														NEGATIVE					POSITIVE
68	543416		NEGATIVE													POSITIVE		POSITIVE		
69	556253		POSITIVE	POSITIVE			POSITIVE													
70	571124		POSITIVE	POSITIVE		POSITIVE											POSITIVE			
71	572242																			
72	591261		POSITIVE	POSITIVE																
73	592438		POSITIVE	POSITIVE																
74	596204		POSITIVE IN MAST CELLS																	
75	565720		NEGATIVE	NEGATIVE																
76	609360	POSITIVE	NEGATIVE		NEGATIVE	POSITIVE									NEGATIVE					
77	238777	FOCAL POSITIVE		NEGATIVE		DIFFUSE POSITIVE											CYTOPLASMIC POSITIVE			
78	614698		NEGATIVE	NEGATIVE																
79	611649		POSITIVE	POSITIVE																
80	634063		NEGATIVE	NEGATIVE																
81	610681		POSITIVE	POSITIVE																
82	638843		NEGATIVE	NEGATIVE																
83	744829				NEGATIVE															
84	643289		NEGATIVE	POSITIVE																
85	642112	POSITIVE			FOCAL POSITIVE	POSITIVE											POSITIVE			
86	648578					NEGATIVE					NEGATIVE			NEGATIVE						
87	657908																			
88	664643		POSITIVE	POSITIVE																
89	665371		POSITIVE	POSITIVE																
90	666679	NEGATIVE	NEGATIVE														CYTOPLASMIC POSITIVITY			
91	674583		FOCAL POSITIVE	FOCAL POSITIVE																
92	669708	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE											CYTOPLASMIC POSITIVE			
93	678585	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE												CYTOPLASMIC POSITIVE			
94	680181		POSITIVE	POSITIVE																
95	679504	NEGATIVE			NEGATIVE												CYTOPLASMIC POSITIVE			FOCAL POSITIVE
96	676775															NEGATIVE		POSITIVE		
97	688430					POSITIVE		NEGATIVE	FOCAL POSITIVE					FOCAL POSITIVE						
98	227263		NEGATIVE																	
99	693791																POSITIVE			
100	590437															WEAK POSITIVE		NEGATIVE		

Sr. No.	MRD No.	P63	CK-7	CK-20	CALRETININ	INHIBIN A	GFAP	TTF-1	CK8/18	P16	P53	CD63	MDM2	H-CALDESMON	CD20	ALK-1	NSE	PAX 8	CYCLIN D1	MIB-1 (%)	FINAL IHC DIAGNOSIS
51	455294																			<1	LEIOMYOMA
52	452123																			15	MYOFIBROBLASTIC SARCOMA
53	458843	NEGATIVE																		75	EWING'S SARCOMA/PNET
54	467180																				EWING'S SARCOMA/PNET
55	459058																			5	SYNOVIAL SARCOMA
56	464296																			35	MALIGNANT FIBROUS HISTIOCYTOMA
57	474600																			4	LIPOSARCOMA
58	489805								NEGATIVE											20	SYNOVIAL SARCOMA
59	475490																			1	FIBROMATOSIS
60	487546																			<1	SCHWANNOMA
61	497692																			20	SYNOVIAL SARCOMA
62	148733									POSITIVE	NEGATIVE									7	LEIOMYOSARCOMA
63	507844																			5	DERMATOFIBROSARCOMA PROTUBERANS
64	81273																			15	SYNOVIAL SARCOMA
65	522160																			2	GASTROINTESTINAL STROMAL TUMOR
66	440563				NEGATIVE	NEGATIVE														3	LEIOMYOMA
67	552125																			<1	BENIGN FIBROUS HISTIOCYTOMA
68	543416																			1	ENDOMETRIAL STROMAL SARCOMA
69	556253					NEGATIVE														30	GASTROINTESTINAL STROMAL TUMOR
70	571124																			4	GASTROINTESTINAL STROMAL TUMOR
71	572242																			2	NODULAR FASCIITIS
72	591261																			20	GASTROINTESTINAL STROMAL TUMOR
73	592438																			5	GASTROINTESTINAL STROMAL TUMOR
74	596204						NEGATIVE													3	NEUROFIBROMA
75	565720																			25	LEIOMYOSARCOMA
76	609360				NEGATIVE															8	SYNOVIAL SARCOMA
77	238777											FOCAL POSITIVE								4	SOLITARY FIBROUS TUMOR
78	614698																			8	LEIOMYOSARCOMA
79	611649																			3	GASTROINTESTINAL STROMAL TUMOR
80	634063																			30	LEIOMYOSARCOMA
81	610681																			30	GASTROINTESTINAL STROMAL TUMOR
82	638843																				LEIOMYOSARCOMA
83	744829												NEGATIVE							35	LEIOMYOSARCOMA
84	643289																			2	GASTROINTESTINAL STROMAL TUMOR
85	642112				NEGATIVE															1	SYNOVIAL SARCOMA
86	648578																			98	ALVEOLAR RHABDOMYOSARCOMA
87	657908																			<1	GLOMUS TUMOR
88	664643																			30	GASTROINTESTINAL STROMAL TUMOR
89	665371																			10	GASTROINTESTINAL STROMAL TUMOR
90	666679				NEGATIVE					POSITIVE										15	LIPOSARCOMA
91	674583																			10	GASTROINTESTINAL STROMAL TUMOR
92	669708				NEGATIVE	NEGATIVE														20	MALIGNANT SOLITARY FIBROUS TUMOR
93	678585																			70	LEIOMYOSARCOMA
94	680181																			3	GASTROINTESTINAL STROMAL TUMOR
95	679504																			45	LEIOMYOSARCOMA
96	676775																			40	LEIOMYOSARCOMA
97	688430																			45	EWING'S SARCOMA/PNET
98	227263																			15	SOLITARY FIBROUS TUMOR
99	693791																			4	DESMOID FIBROMATOSIS
100	590437																			2	LEIOMYOMA

Sr. No.	MRD No.	IHC No.	Sur. Path. No.	Initial name	Age	sex	Site of biopsy	Type of biopsy	Histological diagnosis	VIMENTIN	DESMIN	CYTOKERATIN	MYOGENIN	SMA	S-100	CD-34
101	693605	191/2019	3109/2019	GD	32	FEMALE	LEFT ARM SWELLING	CORE BIOPSY	NEUROGENIC TUMOR		NEGATIVE		NEGATIVE	NEGATIVE POSITIVE	POSITIVE	
102	699456	204/2019	3479/2019	RAJESH	56	MALE	LEFT GROIN SWELLING	EXCISIONAL	SPINDLE CELL TUMOR	POSITIVE	NEGATIVE			POSITIVE	NEGATIVE	POSITIVE
103	703603	228/2019	3825/2019	KARAN	31	MALE	SWELLING LEFT CHEEK	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE
104	708006	240/2019	4070/2019	SD	62	FEMALE	LEFT ADENEXAL MASS	EXCISIONAL	CELLULAR SPINDLE CELL NEOPLASM					POSITIVE	NEGATIVE	NEGATIVE
105	688492	248/2019	3245/2019	TARLOCHAN	59	MALE	LEFT FOOT SWELLING	EXCISIONAL	BENIGN MESENCHYMAL TUMOR POSSIBLY LEIOMYOMA		POSITIVE			POSITIVE	NEGATIVE	POSITIVE
106	721349	275/2019	5081/2019	SB	22	FEMALE	LEFT ZYGOMATIC ARCH	CORE BIOPSY	MALIGNANT ROUND CELL TUMOR	POSITIVE	NEGATIVE		NEGATIVE			
107	708889	280/2019	4290/2019	RC	76	MALE	LEFT CHEST WALL TUMOR	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE		NEGATIVE	FOCAL POSITIVE	WEAK POSITIVE	NEGATIVE
108	677624	285/2019	4944/2019	SEEMA	48	FEMALE	LEFT MIDDLE FINGER	EXCISIONAL	GLOMUS TUMOR			NEGATIVE		POSITIVE		POSITIVE
109	724230	302/2019	5287/2019	BK	50	FEMALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	POSITIVE		NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
110	731327	338/2019	5973/2019	MK	42	FEMALE	UTERUS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE		POSITIVE		POSITIVE		NEGATIVE
111	719113	342/2019	4963/2019	JK	75	FEMALE	RETROPERITONEAL MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	
112	727038	343/2019	5522/2019	NR	42	FEMALE	UTERUS	EXCISIONAL	ENDOMETRIAL STROMAL SARCOMA		NEGATIVE			NEGATIVE		NEGATIVE
113	709046	344/2019	5072/2019	IB	43	FEMALE	THIGH MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
114	736114	383/2019	6494/2019	BJ	90	MALE	RETROPERITONEAL MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	
115	741269	191/2019	6785/2019	GS	71	MALE	RIGHT INGUINAL LYMPH NODE	CORE BIOPSY	METASTATIC DEPOSITS OF POORLY DIFFERENTIATED TUMOR	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE
116	535617	446/2019	8916/2018	SS	75	MALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE	NEGATIVE		NEGATIVE	POSITIVE	NEGATIVE	POSITIVE
117	26193	854/2020	7168/2020	VS	55	FEMALE	JEJUNAL MASS	EXCISIONAL	BENIGN NEUROGENIC TUMOR					NEGATIVE	POSITIVE	
118	982250	888/2020	7554/2020	DS	19	MALE	RIGHT POPLITEAL FOSSA MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR POSSIBLY SYNOVIAL SARCOMA		NEGATIVE	POSITIVE IN EPITHELIAL CELLS		NEGATIVE		
119	981440	891/2020	7569/2020	HS	15	MALE	LEFT LUNG MASS	EXCISIONAL	SPINDLE CELL TUMOR		NEGATIVE	NEGATIVE		NEGATIVE	NEGATIVE	NEGATIVE
120	980517	905/2020	7399/2020	MP	57	MALE	DJ FLEXOR GROWTH	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR ? GASTROINTESTINAL STROMAL TUMOR ? LEIOMYOMA		NEGATIVE			POSITIVE		
121	982506	935/2020	7776/2020	KK	66	FEMALE	RIGHT MAXILLA	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR				NEGATIVE	FOCAL POSITIVE	NEGATIVE	NEGATIVE
122	990643	947/2020	8168/2020	HK	62	FEMALE	LEFT GLUTEAL MASS	EXCISIONAL	MALIGNANT NEOPLASM	POSITIVE	NEGATIVE	WEAK POSITIVE		POSITIVE	FOCAL POSITIVE	NEGATIVE
123	996081	968/2020	8450/2020	AJ	47	FEMALE	RIGHT INDEX FINGER	EXCISIONAL	SPINDLE CELL LESION	POSITIVE	NEGATIVE			WEAK POSITIVE	NEGATIVE	NEGATIVE
124	998238	991/2020	8705/2020	MS	65	MALE	LEFT UPPER THIGH	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	POSITIVE	NEGATIVE		POSITIVE	NEGATIVE	NEGATIVE
125	997153	996/2020	8534/2020	BS	74	MALE	SIGMOID COLON AND SMALL INTESTINE	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR					POSITIVE	NEGATIVE	
126	989936	1001/2020	8049/2020	SK	50	FEMALE	OVARIAN MASS	EXCISIONAL	SEX CORD STROMAL TUMOR POSSIBLE CELLULAR FIBROMA	POSITIVE	NEGATIVE			POSITIVE		
127	999797	1005/2020	8627/2020	SD	75	FEMALE	PERIGASTRIC MASS	CORE BIOPSY	SPINDLE CELL TUMOR					WEAK POSITIVE	NEGATIVE	POSITIVE
128	996991	1027/2020	8579/2020	IK	60	FEMALE	THIGH MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR WITH PROMINENT MYXOID CHANGE	POSITIVE	NEGATIVE			POSITIVE	NEGATIVE	NEGATIVE
129	945855	1029/2020	7775/2020	PL	60	MALE	RENAL MASS	CORE BIOPSY	SPINDLE CELL MESENCHYMAL TUMOR	POSITIVE				FOCAL WEAK POSITIVE	NEGATIVE	
130	1000475	1032/2020	8710/2020	AJ	22	MALE	SWELLING OVER RIGHT HAND	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR POSSIBLY ANGIOFIBROMA	POSITIVE				POSITIVE		
131	873047	23/2020	15525/2019	BK	44	MALE	THIGH MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR		POSITIVE		NEGATIVE	POSITIVE	FOCAL WEAK POSITIVE	NEGATIVE
132	902731	161/2020	2161/2020	SS	72	MALE	LESION OVER TIP OF NOSE	EXCISIONAL	MESENCHYMAL TUMOR	POSITIVE				FOCAL POSITIVE	NEGATIVE	FOCAL POSITIVE
133	908104	207/2020	2415/2020	RN	62	MALE	SWELLING ON BACK	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR		NEGATIVE			NEGATIVE	FOCAL POSITIVE	NEGATIVE
134	911833	243/2020	2715/2020	ANWAR	48	MALE	JEJUNAL MASS	EXCISIONAL	SPINDLE CELL TUMOR					POSITIVE	NEGATIVE	POSITIVE
135	923156	297/2020	3526/2020	NM	27	FEMALE	MANDIBULAR MASS	CORE BIOPSY	SMALL ROUND CELL TUMOR		NEGATIVE	NEGATIVE	NEGATIVE			
136	923559	300/2020	3573/2020	SAKSHAM	2	MALE	PELVIC MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR		POSITIVE		POSITIVE		NEGATIVE	
137	928801	414/2020	4042/2020	MS	14	MALE	SWELLING OVER POSTERIOR ASPECT OF RIGHT THIGH	EXCISIONAL	MESENCHYMAL TUMOR ? FIBROMATOSIS		NEGATIVE			FOCAL POSITIVE	FOCAL POSITIVE	NEGATIVE
138	374939	435/2020	4400/2020	SJ	33	FEMALE	VULVAL CYST	EXCISIONAL	MESENCHYMAL TUMOT LIKELY FIBROHISTIOCYTIC IN ORIGIN				NEGATIVE	FOCAL POSITIVE	NEGATIVE	POSITIVE
139	932753	449/2020	4494/2020	KK	42	FEMALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR					NEGATIVE	NEGATIVE	POSITIVE
140	928325	456/2020	4345/2020	SR	55	FEMALE	FOOT MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR ? SYNOVIAL SARCOMA		NEGATIVE	NEGATIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	
141	924980	479/2020	4418/2020	KS	64	MALE	RETROPERITONEAL MASS	CORE BIOPSY	SPINDLE CELL MESENCHYMAL TUMOR		NEGATIVE			NEGATIVE	DIFFUSE POSITIVE	NEGATIVE
142	937128	495/2020	4758/2020	PK	58	FEMALE	ABDOMINAL MASS	CORE BIOPSY	POORLY DIFFERENTIATED MALIGNANCY	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	WEAK POSITIVE	NEGATIVE	NEGATIVE
143	938007	533/2020	4725/2020	BS	65	MALE	SMALL INTESTINE	EXCISIONAL	MESENCHYMAL TUMOR		NEGATIVE			FOCAL POSITIVE	NEGATIVE	POSITIVE
144	749789	565/2020	5209/2020	HARBHAJAN	59	MALE	SMALL INTESTINE	EXCISIONAL	MESENCHYMAL TUMOR		NEGATIVE			FOCAL POSITIVE	NEGATIVE	NEGATIVE
145	943249	568/2020	5260/2020	BS	74	MALE	RIGHT KNEE MASS	CORE BIOPSY	MESENCHYMAL TUMOR WITH MYXOID CHANGE	POSITIVE	NEGATIVE			NEGATIVE	POSITIVE	NEGATIVE

Sr. No.	MRD No.	Bcl-2	C-KIT	DOG-1	EMA	CD-99	WT-1	SYNAPTOPHYSIN	CHROMOGRANIN A	Tdt	CD-3	CD-7	PAX-5	LCA(CD45)	HMB 45	CD-10	BETA CATENIN	ER	PR	CD-68
101	693605		NEGATIVE													NEGATIVE				
102	699456	NEGATIVE															NEGATIVE			
103	703603				NEGATIVE									NEGATIVE	NEGATIVE					POSITIVE IN MACROPHAGES
104	708006		POSITIVE	POSITIVE																
105	688492																NEGATIVE			
106	721349					POSITIVE						NEGATIVE		NEGATIVE						
107	708889																			POSITIVE
108	677624																			
109	724230		POSITIVE	POSITIVE																
110	731327															POSITIVE		POSITIVE		
111	719113		NEGATIVE	NEGATIVE																
112	727038															POSITIVE		POSITIVE		
113	709046	NEGATIVE																		
114	736114		NEGATIVE	NEGATIVE																
115	741269													NEGATIVE						
116	535617		NEGATIVE	POSITIVE																
117	26193		NEGATIVE	NEGATIVE																
118	982250	POSITIVE IN SPINDLE CELLS																		
119	981440	NEGATIVE			NEGATIVE						POSITIVE IN INFILTRATING T LYMPHOCYTES		NEGATIVE	WEAK POSITIVE						POSITIVE IN SHEETS OF HISTIOCYTES
120	980517		POSITIVE	POSITIVE																
121	982506																			
122	990643	NEGATIVE													NEGATIVE					
123	996081																NEGATIVE			
124	998238																			
125	997153		POSITIVE	POSITIVE																
126	989936			NEGATIVE			NEAGTIVE													
127	999797		POSITIVE	POSITIVE																
128	996991																			
129	945855	NEGATIVE		POSITIVE												NEGATIVE				
130	1000475																			
131	873047																			NEGATIVE
132	902731																			
133	908104																CYTOPLASMIC POSITIVE			
134	911833		POSITIVE	POSITIVE																
135	923156					POSITIVE		NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE			NEGATIVE						
136	923559																			
137	928801																POSITIVE			
138	374939																			
139	932753		POSITIVE	POSITIVE																
140	928325	POSITVE			FOCAL POSITIVE															
141	924980																			
142	937128		NEGATIVE	NEGATIVE	NEGATIVE															
143	938007		POSITIVE	POSITIVE																
144	749789		POSITIVE	POSITIVE																
145	943249																			

Sr. No.	MRD No.	P63	CK-7	CK-20	CALRETININ	INHIBIN A	GFAP	TTF-1	CK8/18	P16	P53	CD63	MDM2	H-CALDESMON	CD20	ALK-1	NSE	PAX 8	CYCLIN D1	MIB-1 (%)	FINAL IHC DIAGNOSIS
101	693605																			7	SCHWANNOMA
102	699456										POSITIVE									10	DERMATOFIBROSARCOMA PROTUBERANS
103	703603																			7	FIBROSARCOMATOUS DERMATOFIBROSARCOMA PROTUBERANS
104	708006																			10	GASTROINTESTINAL STROMAL TUMOR
105	688492																			1	ANGIOLEIOMYOMA
106	721349														NEGATIVE					95	EWING'S SARCOMA/PNET
107	708889																			40	DEDIFFERENTIATED LIPOSARCOMA
108	677624	NEGATIVE																		<1	GLOMUS TUMOR
109	724230				NEGATIVE	NEGATIVE														20	GASTROINTESTINAL STROMAL TUMOR
110	731327									POSITIVE	POSITIVE		POSITIVE							80	LEIOMYOSARCOMA
111	719113												NEGATIVE							40	LEIOMYOSARCOMA
112	727038																			5	ENDOMETRIAL STROMAL SARCOMA
113	709046												POSITIVE							50	DEDIFFERENTIATED LIPOSARCOMA
114	736114												NEGATIVE							85	LEIOMYOSARCOMA
115	741269												POSITIVE							25	EPITHELIOD ANGIOSARCOMA
116	535617																			1	GASTROINTESTINAL STROMAL TUMOR
117	26193																			5	SCHWANNOMA
118	982250																			70	SYNOVIAL SARCOMA
119	981440														POSITIVE IN LYMPHOID CELLS					2	INFLAMMATORY MYOFIBROBLASTIC TUMOR
120	980517																			2	GASTROINTESTINAL STROMAL TUMOR
121	982506												NEGATIVE	POSITIVE		POSITIVE				30	INFLAMMATORY MYOFIBROBLASTIC TUMOR
122	990643													NEGATIVE			POSITIVE			50	MALIGNANT PERIPHERAL NERVE SHEATH TUMOR
123	996081																			<1	FIBROMA
124	998238																			70	LEIOMYOSARCOMA
125	997153																			2	GASTROINTESTINAL STROMAL TUMOR
126	989936				NEGATIVE	NEGATIVE								POSITIVE							LEIOMYOMA
127	999797																				GASTROINTESTINAL STROMAL TUMOR
128	996991													POSITIVE						20	MYXOID LEIOMYOSARCOMA
129	945855																			5	GASTROINTESTINAL STROMAL TUMOR
130	1000475																				ANGIOFIBROMA
131	873047												NEGATIVE							70	LEIOMYOSARCOMA
132	902731																			10	EPITHELIOID HEMANGIOENDOTHELIOMA
133	908104									NEGATIVE			POSITIVE							20	MYXOID LIPOSARCOMA
134	911833																			35	GASTROINTESTINAL STROMAL TUMOR
135	923156							NEGATIVE							NEGATIVE					40	EWING'S SARCOMA/PNET
136	923559																			40	RHABDOMYOSARCOMA
137	928801																			3	FIBROMATOSIS
138	374939																			10	DERMATOFIBROSARCOMA PROTUBERANS
139	932753																			2	GASTROINTESTINAL STROMAL TUMOR
140	928325												NEGATIVE							25	SYNOVIAL SARCOMA
141	924980												NEGATIVE							6	SCHWANNOMA
142	937128																			50	PLEOMORPHIC SARCOMA
143	938007																			10	GASTROINTESTINAL STROMAL TUMOR
144	749789																			8	GASTROINTESTINAL STROMAL TUMOR
145	943249												NEGATIVE							5	SCHWANNOMA

Sr. No.	MRD No.	IHC No.	Sur. Path. No.	Initial name	Age	sex	Site of biopsy	Type of biopsy	Histological diagnosis	VIMENTIN	DESMIN	CYTOKERATIN	MYOGENIN	SMA	S-100	CD-34
146	944809	588/2020	5432/2020	VD	46	FEMALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR						NEGATIVE	
147	926543	589/2020	4963/2020	JR	47	MALE	LARGE INTESTINAL MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR		FOCAL POSITIVE			POSITIVE	NEGATIVE	
148	939808	594/2020	5203/2020	AK	34	FEMALE	SWELLING LEFT ARM	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR POSSIBLY MALIGNANT PERIPHERAL NERVE HSEATH TUMOR		NEGATIVE			NEGATIVE	POSITIVE	POSITIVE
149	945200	601/2020	5465/2020	FA	59	MALE	STOMACH	EXCISIONAL	MESENCHYMAL TUMOR						NEGATIVE	
150	942008	605/2020	5281/2020	RS	51	FEMALE	VULVAL MASS	EXCISIONAL	MESENCHYMAL TUMOR WITH HIGH MITOSIS		NEGATIVE			NEGATIVE	NEGATIVE	POSITIVE
151	921021	355/2020	3651/2020	SD	55	FEMALE	ABDOMINOPELVIC MASS	EXCISIONAL	SPINDLE CELL TUMOR		POSITIVE			POSITIVE		
152	946658	642/2020	5613/2020	NIRMALJIT	29	FEMALE	LEFT INGUINAL MASS	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR POSSIBLY FIBROMATOSIS		NEGATIVE			FOCAL POSITIVE	NEGATIVE	NEGATIVE
153	950544	673/2020	5761/2020	TG	37	FEMALE	RIGHT PARASPINAL MASS	INCISIONAL	SPINDLE CELL TUMO POSSIBLY NEUROFIBROMA					NEGATIVE	POSITIVE	
154	953805	674/2020	5932/2020	SANGEETA	38	FEMALE	STOMACH	EXCISIONAL	SPINDLE CELL TUMOR					NEGATIVE	NEGATIVE	POSITIVE
155	32083	731/2020	6317/2020	GK	75	FEMALE	OMENTAL BIOPSY	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR		NEGATIVE			POSITIVE	NEGATIVE	NEGATIVE
156	806403	769/2020	6702/2020	KAMLESH	59	FEMALE	PELVIC MASS	CORE BIOPSY	MALIGNANT NEOPLASM	POSITIVE	NEGATIVE	WEAK FOCAL POSITIVE				
157	972747	797/2020	6850/2020	PK	46	FEMALE	LUNG BIOPSY	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	FOCAL POSITIVE	NEGATIVE		WEAK POSITIVE	NEGATIVE	
158	906393	181/2020	2394/2020	SS	59	FEMALE	ABDOMINOPELVIC MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR		POSITIVE			POSITIVE	NEGATIVE	NEGATIVE
159	895714	136/2020	2011/2020	BS	73	MALE	RETROPERITONEAL MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	POSITIVE			POSITIVE	NEGATIVE	NEGATIVE
160	903134	155/2020	1997/2020	SHEENU	28	FEMALE	LEFT THIGH MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE	FOCAL POSITIVE	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE
161	870763	001/2020	15333/2019	GEETA	60	FEMALE	PLEURA	CORE BIOPSY	SPINDLE CELL LESION	POSITIVE		NEGATIVE		NEGATIVE	NEGATIVE	POSITIVE
162	833441	180/2020	2070/2020	SS	44	MALE	SWELLING BACK OF NECK	EXCISIONAL	ATYPICAL LIPOMATOUS TUMOR						POSITIVE	NEGATIVE
163	874550	93/2020	001/2020	SC	50	MALE	JEJUNAL MASS	EXCISIONAL	SPINDLE CELL TUMOR		NEGATIVE			POSITIVE	NEGATIVE	NEGATIVE
164	776984	19/21	8901/2020	HK	73	FEMALE	LUNG BIOPSY	CORE BIOPSY	SPINDLE CELL NEOPLASM		NEGATIVE	NEGATIVE		NEGATIVE	POSITIVE	NEGATIVE
165	1004581	29/2021	9093/2020	SJ	30	MALE	LARGE INTESTINAL MASS	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			NEGATIVE		NEGATIVE
166	1006720	34/2021	246/2021	DK	50	MALE	RIGHT INGUINAL REGION MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE				POSITIVE	NEGATIVE	NEGATIVE
167	1010944	60/2021	260/2021	HP	35	MALE	ILEAL MASS	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR							NEGATIVE
168	996907	82/2021	131/2021	SB	43	FEMALE	RIGHT ILIAC FOSSA MASS	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR					NEGATIVE	POSITIVE	NEGATIVE
169	826032	89/2021	8778/2020	BG	74	MALE	NODULE OVER STOMACH	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR					FOCAL POSITIVE	NEGATIVE	POSITIVE
170	969784	96/2021	6720/2020	PS	82	MALE	JEJUNAL MASS	EXCISIONAL	MESENCHYMAL TUMOR					POSITIVE	NEGATIVE	NEGATIVE
171	1031308	217/2021	1583/2021	RL	54	FEMALE	SUPRACLAVICULAR MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	FOCAL POSITIVE	NEGATIVE		NEGATIVE	NEGATIVE	NEGATIVE
172	846221	461/2021	3709/2021	RK	39	FEMALE	MULTIPLE ABDOMINAL MASSES	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR		POSITIVE			POSITIVE		
173	109484	453/2021	3703/2021	SS	39	FEMALE	PELVIC MASS	EXCISIONAL	MALIGNANT MESENCHYMAL TUMORS		NEGATIVE			POSITIVE	NEGATIVE	NEGATIVE
174	1085377	447/2021	3482/2021	IS	31	MALE	RETROPERITONEAL MASS	EXCISIONAL	ATYPICAL LIPOMATOUS TUMOR/WELL DIFFERENTIATED LIPOSARCOMA						POSITIVE	POSITIVE
175	1079317	410/2021	3276/2021	NB	51	FEMALE	UTERUS	EXCISIONAL	MESENCHYMAL TUMOR		POSITIVE	FOCAL POSITIVE		POSITIVE		
176	977684	404/2021	3165/2021	RK	68	MALE	RIGHT THIGH MASS	EXCISIONAL	ATYPICAL LIPOMATOUS TUMOR	POSITIVE				POSITIVE	POSITIVE	NEGATIVE
177	1078014	387/2021	3212/2021	AMANDEEP	3	FEMALE	ABDOMINAL MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	POSITIVE		FOCAL POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE
178	1057938	364/2021	2633/2021	JS	67	MALE	ULNAR NERVE	EXCISIONAL	VASCULAR NEOPLASM POSSIBLY MYOPERICYTOMA	POSITIVE	FOCAL POSITIVE			DIFFUSE STRONG POSITIVE	NEGATIVE	NEGATIVE
179	1038783	293/2021	2273/2021	RS	61	FEMALE	STOMACH	EXCISIONAL	SPINDLE CELL MESENCHYMAL TUMOR POSSIBLY GIST					NEGATIVE	NEGATIVE	POSITIVE
180	1031999	241/2021	1988/2021	RP	52	MALE	LEFT THIGH MASS	EXCISIONAL	MALIGNANT NEOPLASM	FOCAL POSITIVE		POSITIVE IN EPITHELIAL COMPONENT				
181	1101195	243/2021	3847/2021	DG	60	FEMALE	UTERUS	EXCISIONAL	SPINDLE CELL TUMOR	DIFFUSE POSITIVE IN SARCOMATOUS COMPONENT	POSITIVE			POSITIVE		
182	1011613	234/2021	1501/2021	GS	61	MALE	MAXILLA	EXCISIONAL	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE			FOCAL POSITIVE	FOCAL POSITIVE	NEGATIVE
183	1111102	537/2021	4187/2021	JASWANT	75	FEMALE	LEFT THYROID	CORE BIOPSY	MALIGNANT NEOPLASM	POSITIVE	FOCAL POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	WEAK FOCAL POSITIVE	NEGATIVE
184	1120479	617/2021	4541/2021	MK	35	FEMALE	SUBCUTANEOUS LUMP ARM	CORE BIOPSY	NEUROGENIC TUMOR	POSITIVE				NEGATIVE	POSITIVE	
185	1125181	630/2021	4994/2021	HK	62	FEMALE	LEFT THIGH MASS	CORE BIOPSY	MALIGNANT MESENCHYMAL TUMOR	POSITIVE	NEGATIVE		NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE

Sr. No.	MRD No.	Bcl-2	C-KIT	DOG-1	EMA	CD-99	WT-1	SYNAPTOPHYSIN	CHROMOGRANIN A	Tdt	CD-3	CD-7	PAX-5	LCA(CD45)	HMB 45	CD-10	BETA CATENIN	ER	PR	CD-68
146	944809			POSITIVE																
147	926543		NEGATIVE	NEGATIVE																
148	939808	NEGATIVE																		
149	945200		POSITIVE	POSITIVE																
150	942008																			
151	921021																			
152	946658																POSITIVE			
153	950544				NEGATIVE															
154	953805		FOCAL POSITIVE	POSITIVE																
155	32083		NEGATIVE	NEGATIVE																
156	806403				NEGATIVE			NEGATIVE	NEGATIVE					NEGATIVE		FOCAL POSITIVE		NEGATIVE		
157	972747																	NEGATIVE		
158	906393		NEGATIVE	NEGATIVE																
159	895714																			
160	903134	POSITIVE			NEGATIVE															
161	870763																			
162	833441																			
163	874550		POSITIVE	POSITIVE																
164	776984																			
165	1004581		NEGATIVE	NEGATIVE													POSITIVE			
166	1006720			NEGATIVE																
167	1010944			NEGATIVE																
168	996907																			
169	826032			POSITIVE																
170	969784		POSITIVE	POSITIVE																
171	1031308		NEGATIVE	NEGATIVE																
172	846221															NEGATIVE		POSITIVE		
173	109484																	NEGATIVE		
174	1085377																			
175	1079317															NEGATIVE				
176	977684																			
177	1078014																			
178	1057938																			
179	1038783		POSITIVE	POSITIVE																
180	1031999	FOCAL POSITIVE				FOCAL POSITIVE														
181	1101195																NEGATIVE	POSITIVE		
182	1011613																			
183	1111102																			
184	1120479																			
185	1125181																			

Sr. No.	MRD No.	P63	CK-7	CK-20	CALRETININ	INHIBIN A	GFAP	TTF-1	CK8/18	P16	P53	CD63	MDM2	H-CALDESMON	CD20	ALK-1	NSE	PAX 8	CYCLIN D1	MIB-1 (%)	FINAL IHC DIAGNOSIS
146	944809																			10	GASTROINTESTINAL STROMAL TUMOR
147	926543																			60	LEIOMYOSARCOMA
148	939808												POSITIVE							50	MALIGNANT PERIPHERAL NERVE SHEATH TUMOR
149	945200																			5	GASTROINTESTINAL STROMAL TUMOR
150	942008										POSITIVE		NEGATIVE							60	FIBROSARCOMATOUS DERMATOFIBROSARCOMA PROTUBERANS
151	921021				NEGATIVE	NEGATIVE														1	LEIOMYOMA
152	946658																			3	FIBROMATOSIS
153	950544																			<1	NEUROFIBROMA
154	953805																			3	GASTROINTESTINAL STROMAL TUMOR
155	32083													POSITIVE						60	LEIOMYOSARCOMA
156	806403							NEGATIVE						FOCAL POSITIVE			NEGATIVE	FOCAL POSITIVE	POSITIVE	95	ENDOMETRIAL STROMAL SARCOMA
157	972747													POSITIVE						90	LEIOMYOSARCOMA
158	906393																			20	LEIOMYOSARCOMA
159	895714																			60	LEIOMYOSARCOMA
160	903134																			60	SYNOVIAL SARCOMA
161	870763																				SOLITARY FIBROUS TUMOR
162	833441												POSITIVE							2	WELL DIFFERENTIATED LIPOSARCOMA
163	874550																			2	GASTROINTESTINAL STROMAL TUMOR
164	776984				NEGATIVE															2	SCHWANNOMA
165	1004581																				DESMOID FIBROMATOSIS
166	1006720													POSITIVE							LEIOMYOSARCOMA
167	1010944															NEGATIVE			POSITIVE		INFLAMMATORY MYOFIBROBLASTIC TUMOR
168	996907																			10	SCHWANNOMA
169	826032																				GASTROINTESTINAL STROMAL TUMOR
170	969784																				GASTROINTESTINAL STROMAL TUMOR
171	1031308				NEGATIVE									POSITIVE							LEIOMYOSARCOMA
172	846221													POSITIVE							LEIOMYOSARCOMA
173	109484													POSITIVE						70	LEIOMYOSARCOMA
174	1085377												POSITIVE								LIPOSARCOMA
175	1079317													POSITIVE							LEIOMYOSARCOMA
176	977684												POSITIVE								WELL DIFFERENTIATED LIPOSARCOMA
177	1078014																			60	RHABDOMYOSARCOMA
178	1057938													POSITIVE							MYOPERICYTOMA
179	1038783																			10	GASTROINTESTINAL STROMAL TUMOR
180	1031999		POSITIVE	POSITIVE																	SYNOVIAL SARCOMA
181	1101195													POSITIVE							LEIOMYOMA
182	1011613												NEGATIVE	POSITIVE							LEIOMYOSARCOMA
183	1111102							NEGATIVE										NEGATIVE			PLEOMORPHIC SARCOMA
184	1120479																			5	SCHWANNOMA
185	1125181																			60	MALIGNANT PERIPHERAL NERVE SHEATH TUMOR

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No. BFUHS/2K21p-TH/ 5038

Date 20/1/2021

The Principal,
DMC,Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Kajal,** a student of your college for **MD Pathology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Immunohistochemical spectrum of mesenchymal tumors

Supervisor
Dr. Neena Sood
Prof. & Head,
Dept. of Pathology,
DMCH, Ludhiana.

Co-Supervisor
Dr. Sumit Grover
Assoc. Prof.,
Dept. of Pathology,
DMCH, Ludhiana.

The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

SP Singh

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

IMMUNOHISTOCHEMICAL SPECTRUM OF MESENCHYMAL TUMORS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PATHOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER, 2019

DR. KAJAL

DEPARTMENT OF PATHOLOGY

DAYANAND MEDICAL COLLEGE AND HOSPITAL

LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	Immunohistochemical Spectrum Of Mesenchymal Tumors
For the degree of	MD PATHOLOGY
Name of the candidate	Dr. Kajal
Supervisor	Dr Neena Sood, Professor & Head, Department of Pathology, DMCH, Ludhiana
Co-supervisor(s)	Dr. Sumit Grover, Associate Professor, Department of Pathology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Current World Health Organization classification of tumors of soft tissue arranges these tumors into various groups according to their histological patterns. In today's practice, a general approach to reaching a final diagnosis of soft tissue tumors is to first evaluate clinicoradiologic, histomorphologic, and cytomorphologic features of the tumor to generate some provisional differential diagnosis. These include the potential line of histogenesis and whether the tumor is benign or malignant, and low or high grade. Although molecular/genetic testing is increasingly finding its applications in characterizing soft tissue tumors, currently immunohistochemistry (IHC) still not only plays an indispensable role in defining tumor histogenesis, but also serves as a surrogate marker for underlining molecular/genetic alterations.

Aims & Objectives: To study the immunohistochemical spectrum of mesenchymal tumors .

Material & Methods: soft tissue tumor biopsies received in the Department of pathology, Dayanand medical college and hospital, Ludhiana, will be analysed for histopathological and IHC findings. Descriptive statistical analysis will be performed. This will be a five years study (three and half years retrospective , one and half years prospective)

Clinical Significance: IHC technique is widely used in diagnostics and research, and its applications continue to be extended because of its ease of use, reliability, and versatility. Nowadays (IHC) has become a standard method of diagnosis for surgical pathology. Because of the diversity of diagnoses and often subtle nature of diagnostic criteria, IHC finds particular utility in soft tissue tumors.

Keywords: Immunohistochemistry (IHC) , Mesenchymal tumors / Soft tissue tumors, sarcoma , Histopathology.

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CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"Immunohistochemical Spectrum Of Mesenchymal Tumors"** exist in the Department of Pathology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

The greatest amount of bulk of the body is composed of the cells forming tissues that are considered "*soft tissues*" or connective tissues. These are embryologically derived from the *mesoderm*. Hence, they are often called "*mesenchymal*" *tissues*.

Tumors arising from these are called Mesenchymal tumors. Soft tissue tumors have wide morphological as well as histological variation that can be detected by microscopic examination. As benign soft tissue tumors outnumber their malignant counterpart, these tumors more or less resemble the normal tissues.[1] There are special techniques that have been successfully applied to increase diagnostic accuracy; these include conventional special stains, electron microscopy, immunohistochemistry and cytogenetic /molecular methods. They arise nearly everywhere in the body, the most important locations being the extremities, trunk, abdominal cavity and head and Neck.[1]

There is no known predisposing cause but majority of them arise sporadically. Unlike carcinomas that usually arise from recognized precursor lesions; the origin of sarcomas is unknown. Reports have linked specific genetic, immunodeficiency, viral infection and environmental factors with the development of some sarcomas. Environmental factors (e.g., radiation, herbicides) have been associated with the development of specific types of sarcomas.[2-6] Some sarcomas have a higher predisposition to occur in the setting of familial cancer syndromes (e.g., retinoblastoma syndrome, Li-Fraumeni syndrome, hereditary leiomyomatosis and renal cell carcinoma).[7-10] These observations suggest that both environmental and genetic factors are important in the development of these tumors.

Current World Health Organization (WHO) classification of tumors of soft tissue arranges these tumors into 12 groups according to their histiogenesis as follows: adipocytic, fibroblastic/ myofibroblastic, fibrohistiocytic, smooth muscle, pericytic (perivascular), skeletal-muscle, vascular, chondro-osseous, gastrointestinal stromal, nerve

sheath, uncertain differentiation, and undifferentiated/unclassified.[11] Tumor behavior is classified as benign, intermediate (locally aggressive), intermediate (rarely metastasizing), and malignant. The WHO classifies mesenchymal tumors based on various histological patterns. Adipocytic tumors include lipoma (benign), liposarcoma; Fibroblastic pattern includes myofibroma, fibrosarcoma, Desmoid type fibromatosis; vascular tumors include hemangioma, lymphangioma, angiosarcoma. Soft tissue tumors arising from skeletal muscle are Rhabdomyoma, rhabdomyosarcoma and that arising from smooth muscle include Leiomyoma, leiomyosarcoma. Chondro-osseous type include soft tissue chondroma, chondrosarcoma. Apart from these some soft tissue tumors are of uncertain differentiation, these include Myxomas, synovial sarcoma, primitive neuroectodermal tumor (PNET).[11]

Although pathologically diverse, Mesenchymal tumors frequently exhibit similar clinical presentations and radiological features. Correct histopathological and immunophenotypic diagnosis is therefore crucial.

In today's practice, a general approach to reaching a definitive diagnosis of soft tissue tumors is to first evaluate clinicoradiologic, histomorphologic, and cytomorphologic features of the tumor to generate some pertinent differential diagnoses. These include the potential line of histogenesis and whether the tumor is benign or malignant, and low or high grade. Although molecular/genetic testing is increasingly finding its applications in characterizing soft tissue tumors, currently *immunohistochemistry* still not only plays an indispensable role in defining tumor histogenesis, but also serves as a surrogate for underlining molecular/genetic alterations.

6.2 REVIEW OF LITERATURE

Soft tissue tumors are not a common biopsy material of surgical pathology. Enzinger F.M. & W.W. Weiss 1983, Robbins et al 1994, Myhre Jenson et al 1981 reported an incidence of soft tissue tumors as 0.8-1%, 0.8% and < 2% respectively.

Benign soft tissue tumors are more common than malignant. The most common benign tumors are lipoma (44.5%) followed by hemangioma (14.0%) and schwannoma (5.5%).[12] The bulk of intermediate tumors are formed by fibromatosis, hemangioendothelioma and giant cell tumor of soft tissue. The commonest malignant tumors are sarcomas NOS followed by leiomyosarcoma. The benign tumors are found to be commoner in younger population whereas malignant tumors were seen in 5th to 6th decade. Statistically highly significant correlation is found between age and the category of tumor.The most common site of soft tissue tumors as a whole is head & neck (29.0%) followed by upper limb (25.5%).[12] Among benign tumors, hemangiomas have a predilection for head & neck while lipomas are seen commonly in upper limb. Most favoured site for sarcomas is lower limb, followed by abdomen.

After ~30 years of widespread usage, immunohistochemistry (IHC) has become a standard method of diagnosis for surgical pathology. Because of the diversity of diagnoses and often subtle nature of diagnostic criteria, IHC finds particular utility in soft tissue tumors. The use of progressively small amounts of tissue for diagnosis highlights the importance of this method. The sensitivity and crispness of IHC stains have progressively improved with the advent of new techniques. Traditionally, IHC detects cell-typic markers that characterize cell phenotypes, such as chromogranin for neuroectodermal tissue, myogenin for skeletal muscle, and cytokeratin for epithelium.

However, the advent of genetic discoveries have led to IHC testing for detection of fusion gene products or overexpressed oncogenes associated with deletions and mutations. Immunohistochemistry (IHC) technique is widely used in diagnostics and research, and its

applications continue to be extended because of its ease of use, reliability, and versatility.

The immunohistochemistry technique is used in the search for cell or tissue antigens ranging from amino acids and proteins to infectious agents and specific cellular populations. The technique comprises of two steps:

A: slide preparation (specimen fixation and tissue processing) and stages evolved for the reaction (in order: antigen retrieval, non-specific site block endogenous peroxidase block, primary antibody incubation, and the employment of systems of detection, revealing and counterstaining and also slide mounting and storage)

B: interpretation and quantification of the obtained expression.[13]

Basic panel of antibodies: An initial panel of antibodies is often required in order establish the broad lineage. The initial panel for suspected mesenchymal tumor includes S100, Desmin, cytokeratin, EMA, SMA, Vimentin.

Proliferation-based markers such as Ki-67 can also be used for prognosis and grading, but more standardization is needed. In the same vein, it is emphasized that immuno- histochemical (IHC) evaluation of mesenchymal neoplasms is merely an adjunct to thorough histologic evaluation, not a substitute for it as only histomorphological diagnosis is going to help us to choose from wide variety of markers available based on histological pattern of the tumor. Markers of muscle differentiation are Desmin, Actin, Caldesmon, Calponin. Desmin is a specific marker for myogenic differentiation, detected in almost all Rhabdomyosarcoma (RMS) and Leiomyosarcoma (LMS).

Desmin expression may be seen in myofibroblastic tumors. Markers for intermediate filament proteins are keratins (CK 8,CK18,CK19 etc), Glial Fibrillary Acidic Protein (GFAP), vimentin .Keratins are regularly detected in synovial sarcoma, chordoma, myoepithelial tumors, epithelioid sarcoma and adamantinoma. They are seen less commonly in Leiomyosarcoma, epithelioid angiosarcoma, Ewing sarcoma, and alveolar rhabdomyosarcoma. Vimentin is ubiquitous in soft tissue

tumors, and as such, its utility in diagnosis is limited. Markers for sekeletal muscle differentiation are Myogenin, MYOD1, S100, SOX10. MYOD1 and myogenin are nuclear transcription factors highly specific for striated muscle differentiation. Markers of nerve sheath differentiation are CD56, CD57, Collagen type IV, Laminin, Claudin 1. Epithelial membrane antigen (EMA) is frequently expressed in synovial sarcoma, epithelioid sarcoma, perineuriomas, chordoma, myoepithelial tumors, and plasmacytomas.[14] Other markers include β-catenin, Anaplastic Lymphoma Kinase (ALK) etc. Nuclear β-catenin expression is present in 80% of cases of sporadic desmoid fibromatosis and in 67% of desmoid tumors in patients with FAP.[15-17] The study by van Gaal and colleagues reported overexpression of ALK in 81% of alveolar RMS and 32% of embryonal RMS; copy-number gain of ALK was found in 88% of alveolar RMS and in 52% of embryonal RMS.[18] To summarise, Soft tissue tumors represent a heterogeneous group of neoplasms exhibiting a spectrum of histomorphologies, some with overlapping features, and numerous molecular alterations contributing to their diversity. The classification and diagnosis of soft tissue tumors have improved with recent molecular techniques and IHC. It is important to understand not only the diagnostic utility of these recent technologies but also their potential limits and pitfalls.

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study the Immunohistochemical spectrum of mesenchymal tumors.

7. MATERIALS AND METHODS

Soft tissue tumors biopsies received in the Department of pathology Dayanand medical college and hospital, Ludhiana, will be analysed for histopathological and IHC findings. Slides will be subjected to IHC examination under both low power (10x) and high power (40x).

7.1 Source of Data

This will be a three and half years retrospective and one and half years prospective study to be conducted for five years in the department of pathology, Dayanand Medical College and hospital, Ludhiana. All the specimens of soft tissue tumors received for histopathology and immunohistochemical examination will be analysed.

7.2 METHOD OF COLLECTION OF DATA

Inclusion criteria: All mesenchymal tumors of various organs undergoing immunohistochemistry for definite categorisation.

Exclusion criteria:

1. All other neoplasms
2. Soft tissue tumors where IHC has not been done.

Methodology: Soft tissue biopsies will be received in container containing 10% formalin. Tissue will be processed and stained with heamtoxylin and eosin (H&E) stain. IHC staining of slides prepared from formalin fixed paraffin embedded tissue (FFPET) on the BenchMark Classic Automated system (from Ventana) will be done. Sections from FFPET biopsies are cut using the microtome at 3-4micron thickness and mounted onto SuperFrost Plus slides. For each slide, Ventana labels are then printed which include a unique barcode containing all protocol information. The slides are then loaded onto the BenchMark carousel and read by the Ventana Barcode Reader. The automated Benchmark system puts the slides through a series of user-defined de-paraffinization and antigen retrieval steps before commencing with the antibody staining. The primary antibody is either applied automatically if in a pre-diluted dispenser or otherwise manually titrated onto the slide. The pre-diluted dispensors of the ultraView Universal DAB Detection Kit then provide all reagents

required for staining. The counterstain and post-counterstain comprise Haematoxylin and bluing reagent.

Duration of study: This will be five years study, conducted three and half years retrospective from july 2016 to December 2019 and one and half year prospective from January 2020 to June 2021.

Study Design: This is prospective and retrospective study.

Outcome: IHC findings of soft tissue tumors will be documented according to the protocol.

Statistical Analysis: Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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PROFORMA

Serial No.

IHC No.

Surgical path No.

Name Age Sex

MRD Date

Address Phone no

Radiological and gross findings:

Clinical diagnosis:

Site of biopsy:

Type of biopsy: Excisional. Incisional. Core biopsy.

Type requisition: 1) Diagnosis panel. 2) Selective markers

Histopathological diagnosis:

IHC markers-

Positive :

Negative:

Final IHC diagnosis:

Signature of candidate Signature of supervisor